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Healthcare in Low-resource Settings 2023; volume 11(s1):11172

Article

The three month's dietary brown rice intervention has not significantly decreased levels of CRP, TNF-α, and IL6 of type 2 diabetes mellitus patients

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Abstract

Introduction: The increased quantities of inflammatory biomarkers such as C-Reactive Proteins (CRP), Tumour Necrosis Factor-α (TNF-α), and Interleukin-6 (IL-6) have been reported to be associated with an increased risk of metabolic syndrome including type 2 diabetes mellitus (T2DM). However, brown rice is an alternative dietary food source that is known to have many health benefits including high fibre content. In addition to fibre, brown rice is also reported to have moderate amounts of proteins, unsaturated lipids, several minerals, and a lot of bioactive substances that are highly beneficial to health. This study aims to prove the role of brown rice dietary intervention in the reduction of inflammatory biomarkers in type 2 diabetes mellitus patients.

Design and Methods: This was a cross-sectional study with a post-test conducted on 18 patients with type 2 diabetes mellitus. In the intervention phase I, all type 2 diabetes mellitus patients were given brown rice diet for 3 months and followed by a phase II intervention, in which white rice diet was given to the other group of type 2 diabetes mellitus patients for 3 months. Serum was collected at the end of each intervention stage and then serum for Tumour Necrosis Factor-α, Interleukin-6 and C-Reactive Proteins were analysed by the ELISA method. Statistical analysis of the t-test was conducted in order to determine the differences between the two groups allocated in the study.

Results: At the end of the study, it was found that the levels of C-Reactive Protein, Tumour Necrosis Factor-α, and Interleukin-6 after the brown rice intervention was given to type 2 diabetes mellitus patients, it showed a decreasing trend compared to the white rice intervention although not significantly different ($p = 0.6$, $p = 0.63$, $p = 0.59$, respectively).

Conclusions: This study concluded that the administration of brown rice dietary intervention to patients with type 2 diabetes mellitus for 3 months was able to reduce Tumour Necrosis Factor-α, C-Reactive Proteins, and Interleukin-6 however, the reduction was not significant to influence policy change.

Introduction

Currently, studies on how inflammatory biomarkers have contributed negatively to the health outcomes of patients with type 2 diabetes mellitus are being explored.[1] The increased quantities of inflammatory biomarkers such as C-Reactive Protein,[2] Tumour Necrosis Factor-α, and Interleukin-6 have been reported to be associated with an increased risk of metabolic syndrome including type 2 diabetes mellitus and cardiovascular diseases (CVDs).[3] Type 2 diabetes mellitus is a type of metabolic syndrome that is commonly associated with high C-Reactive Proteins values. According to a recent cohort study, high C-Reactive Protein values, especially in subjects with obesity and hypertension were associated with the risk of developing type 2 diabetes mellitus even after the adjustments were made (p trend = 0.02).[4] Similarly, other studies have also indicated that high C-Reactive Protein was associated with high risk of developing type 2 diabetes mellitus (OR = 1,204 95%CI 1,058-1,371, p = 0.005), also with hypertriglyceridemia (OR = 1,157 95%CI 1,040-1,287, p = 0.007), and metabolic syndrome (OR 1,128 95%CI 1.112-1,375, p < 0.001).[5]

Furthermore, another inflammatory indicator known as Tumour Necrosis Factor (TNF-) also significantly contributes to the development of type 2 diabetes mellitus. Similarly, a cross-sectional study reported that increased levels of tumour necrosis factor in the obese group of type 2 diabetes mellitus patients were strongly associated with HbA1C (r = 0.361, p = 0.003) and HOMA-IR (r = 0.2296, p = 0.017).[6] These results are in support of another study that reported an association between increased Tumour Necrosis Factor and insulin resistance in type 2 diabetes mellitus patients (all p = 0.008).[7]

Meanwhile, Interleukin-6 inflammatory biomarker has also been shown to be associated with the risk of developing type 2 diabetes mellitus. According to a recent study on clients who were likely to develop type 2 diabetes mellitus, it was observed that patients showed an increase in Interleukin-6 levels accompanied

Significance for public health

Diabetes mellitus is recognized globally as a major public health threat. Rice as a staple food for Indonesia, is considered to be the main source of carbohydrate and might be an important part of diabetes mellitus nutrition management. Additionally, current study indicates that brown rice contains bioactive ingredients and could be beneficial to be part of the diet for diabetes mellitus patients. Therefore, this clinical study explores the potential advantages of eating brown rice, particularly in relation to its anti-inflammation properties that are necessary in the fight against diabetes mellitus.

by an increase in insulin resistance.[8] It was further reported that an increase in Interleukin-6 in type 2 diabetes mellitus patients could trigger the emergence of diabetic retinopathy (p = 0.005).[9]

Scientists have observed that brown rice is an alternative dietary food source that has many health benefits including high fibre content which could be beneficial in the fight against type 2 diabetes mellitus in communities. Additionally, brown rice is also reported to have moderate amounts of protein, unsaturated lipids, several minerals, and bioactive substances that are also beneficial to health. In addition, this staple food is also affordable and readily available across the globe hence, could be considered as a potential and reliable alternative food source.[10]

However, the contribution of brown rice in controlling inflammation is currently still low but further study in similar field is encouraged. Additionally, an experimental animal study reported that the administration of fermented brown rice was able to reduce the mRNA expression of several indicators of inflammation.[11] Meanwhile, an in vitro study, reported that the special protein content in brown rice was able to provide an inflammatory-reducing effect as well as the effect of selenium.[12] Further studies are needed to truly optimize the health benefits of eating brown rice especially by patients with type 2 diabetes mellitus.

Therefore, this current study was conducted in order to provide the scientific evidence on the contributions of brown rice in improving inflammatory biomarkers in type 2 diabetes mellitus patients.

Design and Methods

This was a cross-sectional study with a post-test that was conducted on 18 type 2 diabetes mellitus patients. The phase I intervention was giving brown rice dietary intervention to type 2 diabetes mellitus patients for 3 months and followed by a wash-out period for 2 weeks before phase II intervention was carried out. The study was continued to phase II intervention in which white rice dietary intervention was administered to another group of type 2 diabetes mellitus patients for 3 months.

The inclusion criteria for participants were females aged 40-60 years, post-menopausal, nutritional status in the range of BMI = 23-27 kg/m^2, used 1 or a combination of Oral Anti-diabetes Drugs (OAD), willing to be the subject of the study and also willing to sign the informed consent forms. The exclusion criteria in this study were respondents who had heart, kidney, liver, and malignancy disorders. In addition, those respondents who had a history of gastrointestinal disorders requiring long-term medical therapy, were smokers, history of allergies and took antibiotics in the last three months were excluded from participating in this study.

Brown rice dietary intervention was given to type 2 diabetes mellitus patients after conducting balanced nutritional calculations. Participants in stage 1 were given brown rice while those in stage II received white rice. In addition, energy requirements were calculated individually using the Harris-Benedict formula. The energy needs of the current study respondents ranged from 1300 to 1500 kcal/day with the provision of brown rice/white rice around 250-300 grams/day which they were given for 3 consecutive months.

Furthermore, the analysis of serum levels of C-Reactive Proteins, Tumour Necrosis Factor-alpha, and Interleukin-6 was performed at the end of each administration of the brown rice and white rice intervention using the ELISA method. Statistical analysis of different tests using t-test was carried-out with the STATA version 16 program and the results were declared significant if the p-value < 0.05 was recorded.

Results and Discussions

The characteristics of the type 2 diabetes mellitus patients involved in the current study included the age range from 40-60 years with the majority being housewives (72.2%), suffering from type 2 diabetes mellitus for less than 5 years (55.6%) and had never received nutrition education (66.7%). Studies have shown that the prevalence of type 2 diabetes mellitus increase with age with peaks recorded at the age range of 55-64 years however, it decreases when an individual is above 64 years. Furthermore, the results of The Indonesian Baseline Health Research, 2013 and 2018 study indicated that as the age increases, the risk of a person developing type 2 diabetes mellitus also increases.[13]

Additionally, the increase in the prevalence of metabolic diseases such as type 2 diabetes mellitus in the elderly individuals was not only directly related to age but also indirectly related to several risk factors such as central obesity, mitochondrial dysfunction, lipid metabolism disorders, inflammation, cell dysfunction, insulin resistance and metabolism syndrome.[14] Shou (2020), further reported that the ageing process of skeletal muscle can cause insulin resistance through mitochondrial dysfunction, accumulation of Intra Myo Cellular Lipid (IMCL), inflammation, oxidative

Table 1. Distribution of respondents characteristics Kusumastuty *et al.*[16]

Characteristics	N	%
Age		
40-49 years old	3	16,7
50-60 years	15	83,3
Work		
Housewife	13	72,2
Government employees	2	11,1
Private employees	1	5,6
Entrepreneur	2	11,1
Long Suffering DM		
<5 years	10	55,6
5-10 years	8	44,4
History of receiving nutrition education		
Once	6	33,3
Never	12	66,7

Table 2. Comparison of respondents' intake data.

Parameter	Brown Rice Mean ± SD	White Rice Mean ± SD	P-value (*t*-test)
Energy Intake (kcal)	1508.15 ± 104.40	1486.78 ± 121.25	0.356
Carbohydrate intake (% energy)	48.82 ± 2.72	49.60 ± 2.34	0.109

Table 3. Inflammatory Profile Data CRP, TNF-α, IL-6.

Parameter	Brown Rice Mean ± SD	White Rice Mean ± SD	P-value (*t*-test)
CRP (mg/L)	112.1 ± 151.2	142.9 ± 186.8	0.59
TNF-α (ng/L)	194.6 ± 133.2	219.1 ± 144.4	0.60
IL-6 (ng/L)	0.9 ± 0.9	1.1 ± 1.1	0.63

stress, expression of Protein Tyrosine Phosphatase 1B (PTP1B), endoplasmic reticulum stress, decreased autophagy, sarcopenia, and overactive Renin-Angiotensin System (RAS). Again, Intra Myo Cellular Lipid accumulation induce oxidative stress and endoplasmic reticulum stress resulting in inflammation that can lead to insulin resistance.[15]

Based on the history of type 2 diabetes mellitus who never received nutrition education which was at 66.7%, the current study suggests that increasing type 2 diabetes mellitus awareness through nutrition education and self-management would greatly help the affected individuals in controlling their respective conditions. A preliminary study, showed that increased nutrition education interventions in the elderly individuals with type 2 diabetes mellitus were not only able to improve their behaviour, knowledge, and attitudes but also increased the glucose control index during the three months of undergoing through the intervention.[17] Furthermore, another study that investigated the clinical benefits of implementing Diabetes Self-Management Education (DSME), reported an improvement in glucose control and thereby reducing the progression and development of microvascular and macrovascular complications in type 2 diabetes mellitus patients.[18]

In this current study, all respondents were given nutrition dietary interventions according to the needs of each individual. In the intervention stages I and II, there was no significant difference in the amount of energy supplied but the only minor difference that was observed was those participants in stage I received brown rice while those in stage II were given white rice. The actual dietary intake data that was recorded indicated that there was no significant difference in the amount of energy and carbohydrate intake from the two intervention stages and did not significantly affect the measured results of inflammatory biomarkers (Table 2).

Furthermore, the results of the measured inflammatory biomarkers such as C-Reactive Proteins, Tumour Necrosis Factor-α and Interleukin-6 showed decreased quantities in the brown rice dietary group and lower inflammatory biomarker values although, the results were not statistically significantly different to influence policy practice (Table 3).

Although brown rice has a higher bioactive content than white rice such as fibre (5 times), magnesium (7.7 times), potassium (5.7 times), and manganese (1.59 times),[19] however, it did not significantly reduce the inflammatory profile. This inability may be related to the type 2 diabetes mellitus patient's Body Mass Index (BMI) profile which was considered to be overweight and ranged between 23-27 kg/m^2 and total body fat of 83.3% of the total patients body weight.[20] It is known that adipose tissues can act as an endocrine organs and be able to secrete adipokines, leptin hormones[21] and chemokines (MCP-1, IL-10, TNF-α, and IL-6).[22] In addition, Interleukin-6 has been reported as a cytokine with pleiotropic effects on inflammation,[23] immune response and haematopoiesis.[24] Furthermore, Interleukin-6 can also stimulate the production of several acute phase reactants such as C-Reactive Protein and stimulate hepatic lipogenesis associated with obesity[25] and insulin resistance.[26]

However, the limitation of this study is that it was extremely difficult to properly the arrange the eating schedules for both groups of the type 2 diabetes mellitus patients hence, this could have affected the outcomes of the research findings. In addition, some patients from both groups also had the desire to consume unhealthy foods that were not recommended in this study. These findings showed that the best strategy to keep diet adherence is laying on consistency and willingness from each individual.

Conclusions

This study concluded that the administration of brown rice dietary intervention for 3 consecutive months had a reduction trend of inflammatory biomarkers such as C-Reactive Proteins, Tumour Necrosis Factor-α, and Interleukin-6 in type 2 diabetes mellitus patients however, the difference in the studied groups were not statistically significant to influence change in practice. Therefore, further studies are needed to ascertain the potential and significant effects of brown rice dietary intake on reducing inflammatory indicators in type 2 diabetes mellitus patients.

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Key words: Brown rice; type 2 diabetes mellitus; TNF-α; CRP; IL-6.

Acknowledgement: The author would like to thank the Department of Nutrition, Faculty of Medicine, University of Brawijaya

Contributions: All authors contribute equally to this article. FAN, IK, ARC, ANHL, and DH designed and coordinated this study. FAN, IK, and DH analyse the biological essays. ARC and ANHL analyse nutritional intake data. FAN, IK, ARC, ANHL, and DH managed the manuscript together.

Conflict of interest: The authors declare no conflict of interest.

Funding: This study has been funded by Faculty of Medicine, University of Brawijaya No. DIPA-023 17.2.67751212021

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Clinical trials: This study obtained research ethics permit from the Health Research Ethics Commission, Faculty of Medicine, University of Brawijaya No. 143/EC/KEPK/07/2020

Informed consent: Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

Conference presentation: This manuscript was presented in the 2nd International Nursing and Health Sciences Symposium 28-30 October 2021, University of Brawijaya Malang, Indonesia.

Conference presentation: Part of this paper was presented at the 2nd International Nursing and Health Sciences Symposium that took place at the Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.

Received for publication: 3 December 2021.
Accepted for publication: 17 May 2022.

Licensee PAGEPress, Italy
Healthcare in Low-resource Settings 2023; 11(s1):11172
doi:10.4081/hls.2023.11172

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