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Glycemic and Lipid Metabolic Markers in Type 2 Diabetes Mellitus Patients after Consuming Red Pigmented Parboiled Rice as a Staple—A Clinical Trial

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Abstract

Red pigmented rice has been proven to have unique properties beneficial to health. These might be further enriched if parboiled. This study investigated the effects of consumption of RPPR on glycemic response, lipid profile and BMI in diabetics.

For this prospective study patients with diabetes mellitus (aged 40-75 yrs) in a prison (n = 69) were recruited. Their usual diet in prison was red pigmented rice. They were served 180 g of RPPR for 16 weeks during intervention period.

Fasting Plasma Glucose (FPG) and BMI was assessed at 0, 4, 8, 12 weeks and glycated haemoglobin and lipid profile at 0 and 16 weeks. Values at 0 weeks were compared with those at 4, 8, 12, 16 weeks after consuming RPPR using ANOVA repeated measures. HBA_{1c} and lipid profile at 16 weeks were compared with the 0 week value. During consumption of RPPR, FPG was significantly reduced at 8 ($p = 0.006$), 12 ($p = 0.002$), and 16 weeks ($p = 0.005$), with a significant reduction of the BMI at 8 ($p = 0.028$) and 16 weeks ($p = 0.003$). At the end of 16 weeks of consuming RPPR, LDL, Total Cholesterol (TC) and TC/HDL ratio were significantly reduced compared to 0 weeks ($p = 0.001$, $p = 0.013$, $p = 0.032$, respectively. These results suggest that RPPR consumption reduces FPG, LDL, TC,TC/HDL ratio and BMI.

Keywords

glycemic control, lipids, Type 2 Diabetes Mellitus, red pigmented parboiled rice

1. Introduction

Due to increasing obesity rate and westernization of life styles, the prevalence and the incidence of Type 2 Diabetes Mellitus (T2DM) in developing countries are increasing dramatically (Jayawardena et al., 2012). Rice (*Oriza Sativa*) is the staple diet consumed by more than half the world population. Although studies have indicated that white rice consumption is associated with increased risk of T2DM, there are only few interventional studies carried out to identify a healthy rice variety (Hu et al., 2012). Colored rice (black, purple, red, brown) due to its edible pigments deposited in the nutrient containing pericarp of the rice grain is a special entity studied worldwide. Colored rice contains a variety of pigments and bioactive substances. This include numerous anti-oxidant molecules such as phenolic acids, flavonoids, anthocyanins, proanthocy-anidins, tocopherols, tocotrienols and Y-oryzanol, etc. (Nam et al., 2003). As evidenced by epidemiological studies, there might be an association between low incidence of certain chronic diseases amongst rice consumers,which might be due to anti-oxidant compounds in rice (Goufo & Trindade, 2014).

Among the antioxidants, anthocyanin, which is the pigment found in red or purple pericarp of rice, is considered a natural colorants of foods. It is reported that there are unique properties of anthocyanin pigment such as antioxidant activity (Nam et al., 2006), anti-inflammatory (Wang et al., 2007), anticancer (Hyun & Chung, 2004) and hypoglycemic (Takikawa et al., 2010) which makes consuming pigmented rice beneficial for health. Pigmented rice is commonly consumed by people in South East Asia including Sri Lanka, Thailand, China, etc. (Sompong et al., 2011).

Red Pigmented rice is amongst the rice varieties with high activity of antioxidants. Anthocyanins: the pigment in red rice comprised of several types cyanidin 3-glucoside, cyanidin 3-galactoside, cyanidin 3-rutinoside, cyanidin 3,5-diglucoside and malvidin 3-galactoside, etc. (Goufo & Trindade, 2014).

Numerous recent observational studies have evaluated the hypoglycemic effects of anthocyanin. A study conducted in an obese diabetic rat model has found that, anthocyanin suppresses lipogenesis,reduces hepatic steatosis in hepatocytes and plays a role in inhibiting fatty acid synthesis (Guo et al., 2011).

Quality of the red pigmented rice might be enhanced by parboiling. Parboiled rice, obtained after soaking paddy in water, steaming to complete gelatinization and drying, has many advantages over raw rice (Figure 1). Strengthening of kernel integrity, increased milling recovery, prevention of the loss of nutrients during milling, reduced cooking time and improved shelf life as well as prevention of the proliferation of fungi and insects are some of the reasons for the increasing demand for parboiled rice (Hoover, 2010; Patindol et al., 2008). It is claimed that parboiling reduces the glycemic index by almost 30% compared to its non parboiled variety due to starch retrogradation, high soluble fiber content and increased physical hardness of the grain for digestion (Larsen et al., 2000).

Figure 1. Red Pigmented Parboiled Rice

Parboiling of red pigmented rice might have several advantages over other types of rice. Although no significant differences in macronutrient composition among the red pigmented and red pigmented parboiled rice have been observed there were differences in the glycemic indices and the soluble fibre contents (Table 1; Hettiarachchi, 2000). Due to the different levels of anthocyanic pigment differences in the digestibility has also been observed (Perera & Jansz, 2000).

Table 1. Composition and Glycemic Indices of Cooked Red Pigmented and Red Pigmented Parboiled Rice

Nutrient/glycemic index	BW 351	BW272-6B	BW 351*	BW272-6B*
Carbohydrates (g)	73.5	82.6	78	74
Amylose/amylopectine	26.4/47.3 = 0.5	26.4/56.2 = 0.4	29.9/48.1 = 0.6	26.1/47.5 = 0.5
Protein (g)	9.2	11.6	6.7	9.6
Fat (g)	1.5	0.9	1.1	2.1
Total fiber (g)	5.3	2.6	5.7	4.3
Soluble fiber (g)	1.7	1.4	1.9	3.1
Glycemic index	73	68	56	58
Moisture (g)	14.7	13.7	12.2	13.7

Macronutrients are calculated on dry basis. * denotes parboiled rice.

A preliminary *in vitro* study with red pigmented parboiled rice has shown that there is alteration in the pigments in parboiling (Perera & Jansz, 2000). A lower glycemic response in red parboiled rice might be due to protein pigment complex permeating the starch gel causing inhibition of enzyme hydrolysis during parboiling (Perera & Jansz, 2000). Rice pigments and the antioxidant properties have been extensively investigated, yet interventional studies in human testing the physiological effects of red pigmented rice are few.

Owing to certain characteristics postulated such as, presence of anti-oxidants, anti amylase activity and the ability to improve the soluble fibre content after parboiling and lower glyceamic index, consuming red pigmented rice might be beneficial in health as well as in diabetics.

The effect of consumption of red pigmented parboiled rice on lipid markers and BMI has not been ascertained in diabetic patients. Consuming red pigmented parboiled rice might favorably answer an emerging public health problem in the developing world by achieving the expected outcomes of diabetes mellitus in improving the lipid and glucose metabolism markers.

Thus we hypothesized that red pigmented parboiled rice consumption lowers the glycemic response, improves the lipid profile and lowers the BMI in T2DM patients. The aim of this study was to investigate the effect of red parboiled rice consumption on the glycemic control, lipid profile and BMI in T2DM subjects.

2. Method

2.1 Ethics Statement

Ethics Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka specifically approved this study. Permission to conduct the study was obtained from the Commissioner of Prison, Prison Head Quarters, Welikada, Sri Lanka. Informed written consent was obtained from all participants before enrollment to the study and they were given the option of withdrawing from the study at any moment. The study was conducted according to the principles expressed in the Declaration of Helsinki.

2.2 Participants and Study Design

This analytical clinical trial (CTRI/2014/06/004666) was conducted at Welikada prison in Colombo, the capital of Sri Lanka, where more than 2000 prisoners with long-term imprisonment serve their sentences. The study evaluated the effects of pigmented parboiled rice consumption on blood glucose control, BMI and lipid profiles in T2DM patients for a period of 16 weeks. The list of all registered diabetes patients in Welikada prison was obtained from the prison hospital and they were invited for screening through posters displayed at the prison hospital and dispensary. All responded patients were screened according to the inclusion/exclusion criteria and their dietary habits, exercise patterns and presence of complications were assessed by an interviewer administered questionnaire.

Out of 363 registered T2DM patients, 102, T2DM patients fulfilled the inclusion criteria and were recruited for the study following obtaining informed written consent. T2DM patients between the ages of 40 and 75 yrs, those who were not receiving medication for any disease other than diabetes were included.

Those who had complications of diabetes, who received insulin therapy, whose medication regimen was altered during the study, those who had elevated cholesterol levels and blood glucose levels were excluded. Of an initial diabetic population of 102 only 69 were recruited as those patients who had elevated serum cholesterol (n = 12) and elevated FPG (n = 14) were removed from the study sample and referred for treatment and seven subjects opted out from the study. The usual diabetic diet in the prison comprised of cooked red pigmented rice (180 g), starchy vegetable 50 g, leafy vegetable 50 g and fish or meat (100 g). In this intervention red pigmented parboiledrice was served instead of red pigmented rice. At 0 weeks, FPG, lipid profiles, HbA_{1c} and BMI were assessed. These measurements were considered as baseline measurements. FPG and BMI were determined every 4 weeks from the day of commencement of the study whereas lipid profiles, and HbA_{1c} were determined at the end of 16 weeks (Figure 2).

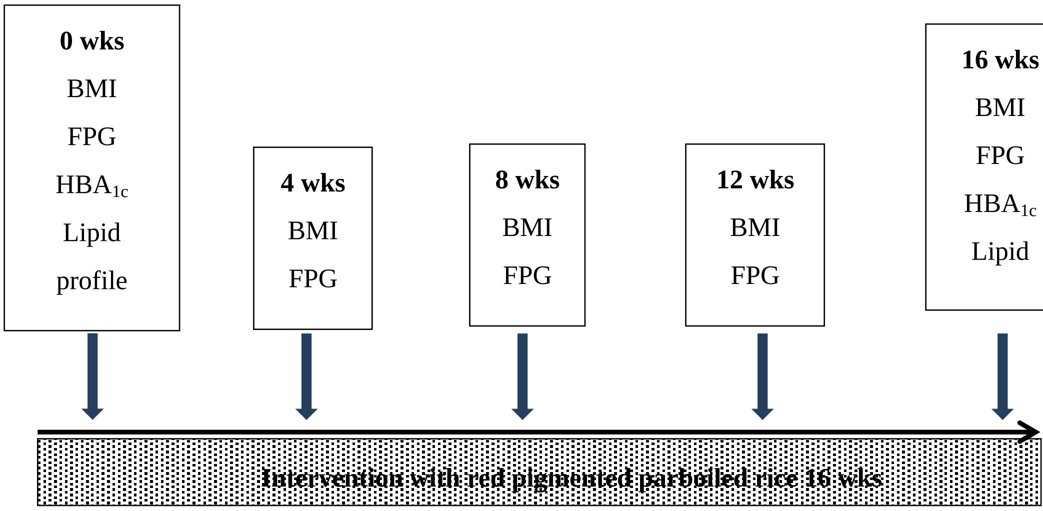

Figure 2. Time Points at Which Biochemical Parameters and BMI Were Assessed

2.2.1 Activities

Prisoners generally have a fixed daily routine of physical activities and all of them were following the same schedule of physical activities.

2.2.2 Medication

Patients on antidiabetic medication (sulfonylurea: n = 18, biguanides: n = 21, thiazolidiones: n = 8, and sulfonileurea + biguanides: n = 22) were included in the study. In case of change in medication during the course of the study, those subjects were removed from the study (n = 0).

2.3 Data Collection

Venous blood was collected after an overnight fast into EDTA tubes, sodium fluoride containing tubes and plain tubes for HbA_{1c}, FPG and lipid profile respectively. Samples were transported immediately to the Nawaloka Metropolis Laboratory, Colombo 2, Sri Lanka and centrifuged at 4000 rpm for 10 minutes. Plasma was stored until analysis at 2-8^{0}C up to a maximum of 1 week, unless analyzed immediately.

2.4 Assessment of BMI and Blood Pressure

Weight was measured using a digital weighting scale (Chyo Mu-150K, Japan), to the nearest 0.1 kg while standing with barefoot on the center of the scale-platform, keeping the hands at sides and looking straight. Height was measured only at 8 weeks to the nearest 0.1 cm, using stadiometer (No. 265M), while standing up straight against the backboard, with barefoot, heels together, toes apart, and the head, shoulder blades, buttocks and heels in contact with the backboard with the head kept in the Frankfurt's horizontal plane. BMI was calculated by determining the weight to height squared ratio. As a base line investigation systolic and diastolic blood pressure was determined using the sphigmomanometer.

2.5 Analytical Methods

Blood samples for FBG were analyzed by glucose oxidase method which is an adaptation of the hexokinase-glucose-6-pospate dehydrogenase method, in a fully automated biochemistry analyzer (SIEMENS Dimension: CT. DF 40 USA).

HbA_{1c} was analyzed by D-10 HbA1c program which utilizes the principles of ion-exchange High-Performance Liquid Chromatography (HPLC), using fully automated analyzer by Immunoturbidimetric method (Roche Hitachi (902) Cobas System) (Yasmeen et al., 2011).

Blood samples for lipid profiles were analyzed by enzymatic method using fully automated SIEMENS Dimension CT. DF 27 (USA) instrument (Flegg, 1973; Rautela & Liedtke, 1978).

2.6 Statistical Analyses

FBG and, BMI, at 0 weeks were compared with values obtained at 4, 8, 12 and 16 weeks (Table 2, Figure 2, Figure 3), using ANOVA repeated measures, General Linear Model (GLM). HbA_{1c} and lipid profiles at 0 weeks were compared with values obtained at 16 weeks (Table 2, Figure 2, Figure 3), using ANOVA repeated measures, GLM. The values at 0 weeks was considered as the baseline for RPPR intervention. All analyses were performed using SPSS (version 17.0) software and a P value < 0.05 was taken as statistically significant.

3. Results

Base line characteristics: The mean (±SEM) age of the study group was 50.72 years (±1.08). There were 17 Females and 52 males in the study group. At 0 weeks Subjects' mean (±SEM) of weight, height and BMI were 62.98 kg (±0.97), 1.62 m (±0.01) and 23.88 kg/m^2 (±0.29), respectively. At 0 weeks their mean (±SEM) diastolic blood pressure was 83.18 (±0.70) and the mean (±SEM) systolic blood pressure was 128.19 (±1.20).

Body weight significantly decreased after consumption of RPPR compared to 0 weeks. Hence BMI was significantly decreased after consumption of RPPR for 8 ($p = 0.028$) and 16 weeks ($p = 0.003$) compared to 0 weeks.

3.1 Glycemic Control

After the intervention with RPPR consumption, FPG was significantly reduced at 8 ($p = 0.006$), 12 ($p = 0.002$), and 16weeks ($p = 0.005$) compared to 0 weeks (Table 2, Figure 3). Although there was a decreasing trend, the HBA_{1c} did not show a significant change at 16 weeks compared to the 0 week value (Table 2).

Table 2. Assessment of Biochemical Parameters and BMI of T2DM after Consuming Red Pigmented Parboiled Rice (n = 69)

Parameter	Consumption of red pigmented parboiled rice at				
	0 weeks	**4 weeks**	**8 weeks**	**12 weeks**	**16weeks**
BMI	23.88 ± 2.39	23.87 ± 2.40	23.82 ± 2.36	23.81 ± 2.30	23.78 ± 2.29
FPG mg/dL	1.12 ± 26.39	1.06 ± 24.25	1.03 ± 18.13	1.02 ± 18.51	1.03 ± 16.95
LDLmg/dL*	1.27 ± 30.11				1.14 ± 27.03
HDLmg/dL*	41.82 ± 10.59				42.47 ± 10.40
TCmg/dL*	1.95 ± 45.02				1.83 ± 37.43
TGmg/dL*	1.63 ± 84.57				1.52 ± 66.16
TC/HDL*	4.93 ± 1.51				4.50 ± 1.27
HbA_{1c} (%)*	6.37 ± 1.40				6.31 ± 1.20

Note. Mean +/-SD. *Parameters were assessed at 0 and 16 weeks.

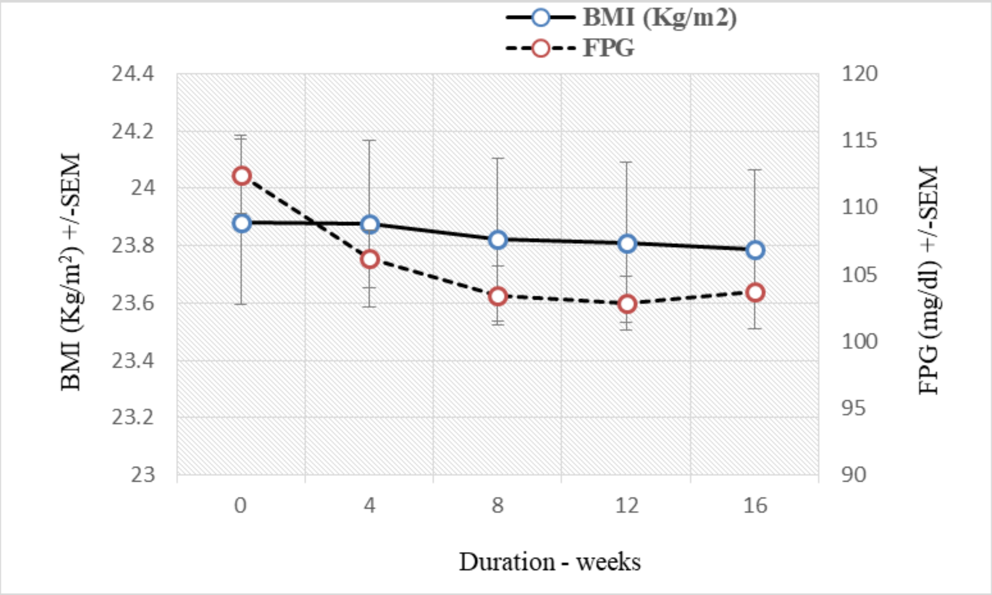

Figure 3. Variations in FPG and BMI during the Intervention Period

3.2 Lipid Profile

At the end of 16weeks of consuming RPPR, LDL (p = 0.001) and TC (p = 0.013) were significantly reduced compared to the 0 weeks value (Table 2, Figure 4). There was no change in the HDL or TG concentration. However the TC/HDL ratio (p = 0.032) was significantly reduced compared to the 0 weeks value.

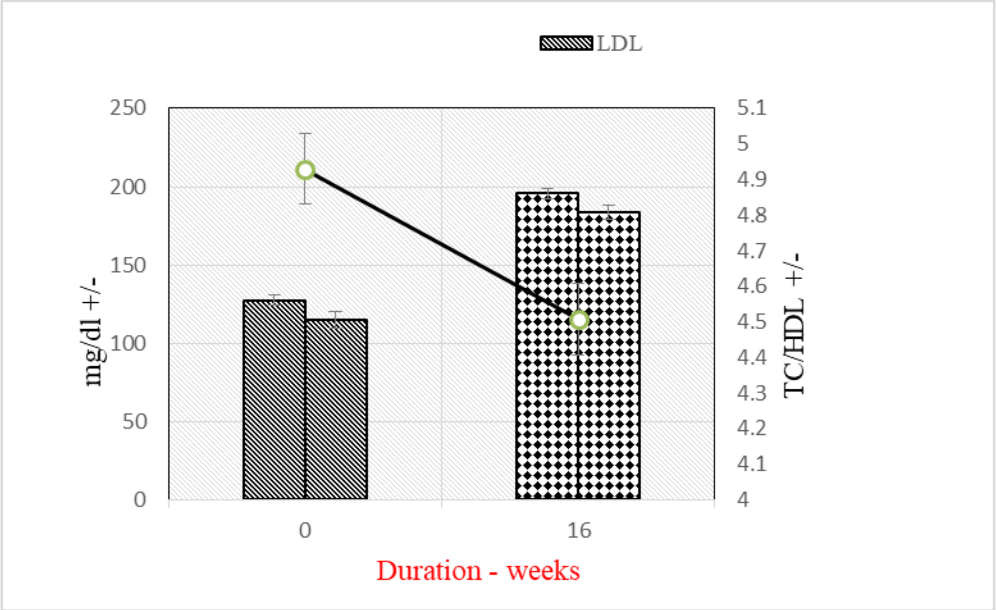

Figure 4. Changes in Lipid Parameters during the Intervention Period

4. Discussion

Investigations to identify rice varieties which produce a low glycemic response have been carried out worldwide. The chemical composition of red rice has been extensively investigated. Anti oxidant and lipid lowering effects of pigmented rice has been reported. However no interventions determining the effect of consuming red pigmented rice were reported on T2DM patients. The present study is the only study to report on glycemic response, lipid profile and BMI on consuming red pigmented parboiled rice in T2DM patients. A reduction in the fasting plasma glucose was seen with RPPR consumption at 4 ($p = 0.236$), 8 ($p = 0.006$), 12 ($p = 0.002$), and 16 (0.005) weekscompared to 0weeks. However at the end of 16 weeks the HbA_{1c} concentration was unchanged in spite of a decreasing trend. Probably consuming RPRR for a longer duration, for more than 16 weeks, might reduce the HbA_{1c} concentration. In contrast during consumption of pre germinated brown rice for 16 weeks in people with impaired glucose tolerance the HbA_{1c} concentration compared to white rice was reduced (Bui et al., 2014). In another study comparing pre germinated brown rice with white rice consumption for a similar time duration, a reduction of fructosamine concentration was observed (Hsu et al., 2008). This may be because in both studies pregerminated brown rice was compared with white rice whereas the present study compared the basal blood glucose concentration. A study which substituted brown rice for white rice for 16 week did not show conclusive evidence in improvement in the metabolic risk factors such as FPG, HBA_{1c}, HDL, TC and TG (Zhang et al., 2011).

Although the brown rice contain a higher fibre content compared to white rice the 16 weeks duration of consumption of brown rice might be inadequate. Similarly even though the fibre content in red pigmented parboiled rice is high to observe a difference in HBA_{1c} probably a the duration of consumption should be more than 16 weeks.

At the end of 16 weeks after consuming of red pigmented parboiled rice lipid markers such as LDL cholesterol (p = 0.001, total cholesterol (p = 0.013) and TC/HDL ratio (p = 0.032) werereduced compared to the basal level. This might be attributed to the presence of anthocyanin in red pigmented rice. Supplementation of anthocyanin for 12 weeksin a double-blind, randomized, placebo-controlled trial in dyslipideamic subjects has shown an improvement in serum LDL- and HDL-cholesterol concentrations (Qin et al., 2009).

As proven by many prospective studies it is clear that the risk of diabetes increases with white rice consumption implying red pigmented parboiled rice might be an alternative for white rice (Villegas et al., 2007).

Consuming pre germinated brown rice compared to white rice, for a period of 16 weeks produced a lower LDL and triglyceride level and significantly higher HDL cholesterol level, in Vietnamese women with impaired glucose tolerance. However the TC concentration was not reduced (Bui et al., 2014). Another study in patients with diabetes and individuals with impaired glucose tolerance in Taiwan also proved the improvement on levels of serum TCl, Tri-Acylglycerol (TG) and HDL-Cholesterol (HDL-C) with pregerminated brown rice for 16 weeks (Hsu et al., 2008). This implies that the changes in the lipid profile occur due to consuming pre germinated brown rice unlike white rice. Thus red pigmented parboiled rice can be suggested as another alternative to be recommended to improve the lipid profile in diabetes mellitus in prison.

It was demonstrated in diabetic rats that the hypocholesterolemic effects of germinated brown rice were partly mediated through the upregulation of the LDL-R and APO A1 genes (Ithnin, 2013). It was shown that the pre germinated brown rice bran contains a Y-oryzanol which are effective in lowering hyperlipideamia (Sugano & Tsuji, 1997). Pre-Germinated Brown Rice (PGBR) is obtained by allowing the rice kernels to slightly germinate once soaked in water. Although it is a common practice in Japan most people might not be familiar in preparing PGBR.

Although a low glycemic indices were found in, easy-cook long-grain rice and white basmati, long term physiological effects of consuming these varieties were not determined (Hsu et al., 2008). Improvement of lipid markers after consuming pre-germinated brown rice for 16 weeks has been also attributed tophysical shape of the rice grain causing delayed digestion and high fibre content (Hsu et al., 2008). It is reported that the glycemic response in rice: is influenced by the physical texture, chemical structure amylose amylopectine ratio and soluble fibre content, anti amylase activity and antioxidants, etc. (Björck & Elmståhl, 2003; Gunaratne et al., 2013). Parboiling of the red pigmented rice has increased in the soluble fibre content, lowered the digestibility and the glycemic index. This might be a added factor which increase its efficacy (Hettiarachchi, 2000; Hettiarachchi et al., 2001; Larsen et al., 2000; Perera & Jansz, 2000).

This prospective study ascertains the efficacy of consuming red pigmented parboiled rice as a staple while maintaining other ingredients in the diet relatively constant. Our hypothesis was tested in a group of people having a generally fixed dietary menu throughout the study period. Due to presence of a fixed dietary menu, and organized daily physical activities of prison in-mates, it was assumed that energy expenditure did not vary in the intervention period as before. Hence reduction of the BMI at 8 weeks ($p = 0.028$) and 16 weeks ($p = 0.003$) compared to basal level might be attributed to consumption of red pigmented parboiled rice.

Similar to consuming red pigmented parboiled, consuming pre germinated brown rice compared to white rice, for a period of 16 weeks produced a significant reduction in the BMI in Vietnamese women with impaired glucose tolerance. Thus red pigmented parboiled rice might be prescribed in patients with diabetes mellitus although the previous study data is from individuals withimpaired glucose tolerance.

Controlling energy expenditure to a scientifically acceptable degree throughout the intervention period was one of the strengths of this study.

Dietary habits of the prison inmates did not vary except for introducing red pigmented parboiled rice and the fact that assessors and lab technicians were blind on the variety of rice were strengths of this study. During the intervention medications were not changed among the final study population which was taken for analysis.

When compared to other intervention studies with rice, the sample size of this study was larger and the total diabetics in the prison were considered and this was strengths of this study.

Firstly due to the financial and time constrains intervention period was limited to 16 weeks and this would have preferably been longer to see changes in HbA_{1c} concentration.

Secondly due to the practical difficulties groups of prison inmates could not be randomized to an intervention and non intervention group. Future randomized clinical trial in diabetics with a longer duration is suggested. To ascertain the actual effect of consuming red pigmented parboiled rice on HbA_{1c} the duration would have to be lengthened to more than 16 weeks.

In conclusion, this study proves that, consuming red pigmented parboiled rice for 16 weeks can significantly reduce the blood glucose level. Furthermore, consuming red pigmented parboiled rice for 16 weeks can produce a significant reduction in the glycemic response, lipid profile and BMI. Due to the impact of red pigmented parboiled rice on these markers this variety might be recommended for T2DM patients. Considering the unique physiological and physiochemical properties as discussed before, further prospective studies may confirm that red pigmented parboiled rice consumption might even besuitable for the general community.

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