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One-week sorghum (*Sorghum bicolor* L.) grain consumption is insufficient to increase adiponectin levels in prediabetic adults

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Objective. Adiponectin is an internally produced bioactive compound with a protective role against the insulin resistance-related diseases. Finding an adiponectin modifier can play a beneficial role in preventing the progression of the diseases, particularly in the prediabetic patients, as a high-risk population. This study was undertaken to examine the effect of dietary sorghum grain for a week on the plasma adiponectin levels in prediabetic patients.

Methods. The study involved 26 (13+13) participants in both control and intervention groups. The control group maintained their habitual diet of white rice, while the intervention group replaced their habitual diet of white rice with sorghum grain for seven consecutive days. In all participants, the adiponectin concentration was measured before and after the intervention period.

Results. Most study subjects had central obesity and dyslipidemia. Adiponectin levels after the intervention period decreased from the baseline in the control and sorghum groups including in all BMI groups. The change of decreasing adiponectin level was greater in the control than the sorghum group and in line with greater BMI in the sorghum group, but statistically insignificant. No significant difference in adiponectin concentrations was found among BMI groups.

Conclusion. Sorghum grain consumption for a week is insufficient to increase adiponectin levels in the prediabetic patients. Insulin resistance, central obesity, and dyslipidemia may be the confounding variables that alter the favorable effect of sorghum on adiponectin. Longer sorghum consumption or other interventions may be needed to increase the adiponectin levels in people under these conditions.

Keywords: adiponectin, body mass index, insulin resistance, prediabetic, sorghum

Adipose tissue is generally recognized as an endocrine organ capable of producing a variety of bioactive compounds that regulate metabolic homeostasis (Coelho et al. 2013). Adiponectin is one of the peptide hormones secreted by adipocytes in adipose tissue that raises many interests because of its critical role in many disease processes. Mediated by two adiponectin receptors (AdipoR1 and AdipoR2), adiponectin exerts many beneficial biological activities, including insulin sensitizers, anti-hyperglycemia, regulator of lipid metabolism, anti-inflammation, anti-atherosclerotic, and suppression of carcinogenesis (Turer and Scherer 2012). Available evidence has suggested that adiponectin level is inversely correlated with diseases related to insulin resistance, such as obesity, type 2 diabetes mellitus (T2DM), cardiovascular disease, and cancer (Nguyen 2020). A recent meta-analysis study involving more than 40 000 participants has reported that circulating adiponectin level is

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significantly lower in prediabetes patients than in healthy controls that might indicate that the level of circulating adiponectin decreases before the onset of diabetes (Lai et al. 2015). This result supports the other cohort-prospective study that has shown a lower serum adiponectin level as an independent predictor of diabetes incidence after 5.5 years of follow-up with an OR of 3.6 (95% CI 1.4–8.6) (Fagerberg et al. 2011). Consequently, strategies to increase the level of adiponectin can play a beneficial role in preventing the progression of T2DM and other insulin resistance-related diseases, particularly in the high-risk population, such as the prediabetic population.

Circulating adiponectin level is affected by numerous factors, including age, sex, genetic factor, physical activity, ethnicity, body mass index (BMI), and dietary factors (Janiszewska et al. 2021). Previous studies have suggested a positive correlation between adherence to the Mediterranean diet and increasing adiponectin levels (Sureda et al. 2018). The Mediterranean diet is characterized by an abundant supply of vegetables, fruits, olive oil, whole-grain cereal products, fatty saltwater fish, moderate alcohol intake, and low red meat consumption. It has been indicated that the bioactive components of the Mediterranean diet (i.e., polyphenols, fibers, vitamins, and omega-3 fatty acids) have a favorable effect on adiponectin expression. Other studies have also reported a significant association between dietary fiber and higher levels of adiponectin, either in the general or diabetic population (Qi et al. 2005; AlEssa et al. 2016). These studies signaled that dietary intervention could play a beneficial role in increasing adiponectin levels.

Sorghum (*Sorghum bicolor* L., Moench) is the fifth most-produced cereal grain crop worldwide. Sorghum grain is primarily used for human consumption in Asia, Africa, and Latin America, while it is used for animal feed in Australia and the US (Xu et al. 2021). However, the use of sorghum for human consumption has been carried out in these countries due to its high nutritional content and its beneficial potential for humans. Sorghum is mainly composed of starch, which is more slowly digested than other cereals so is associated with a lower glycemic index. Sorghum also possesses unsaturated lipids, low-digestibility proteins, minerals, vitamins, and abundant polyphenolic compounds, including phenolic acids, flavonoids, and tannins (de Morais Cardoso et al. 2017).

The review of previous studies summarized by Stefoska-Needham et al. (2015) has demonstrated that phenolic compounds in sorghum can provide many health benefits, including antioxidant, anti-inflammatory, anti-proliferative, anti-diabetic, and anti-atherogenic activities. A previous *in vivo* animal study has reported that adiponectin expression in adipose tissue was significantly higher in mice given 0.5% sorghum extract and 1% sorghum extract than control in mice fed a high-fat diet for 6 weeks. This study has suggested that sorghum might induce over-expression of PPAR-γ and reduce TNF-α expression in adipose tissue that consequently increased the adiponectin expression (Park et al. 2012). Studies evaluating the role of sorghum on adiponectin are still very limited. To the best of our knowledge, currently, no earlier studies are addressing the effect of sorghum on adiponectin levels in humans.

We hypothesized that sorghum grain consumption could also increase the circulating adiponectin levels in prediabetic patients. Thus, the present study was aimed to examine the effect of dietary sorghum grain served for a week on plasma adiponectin levels in prediabetic patients. The comparisons of adiponectin levels pre- and post-intervention period according to BMI categories were also carried out in the present study.

Materials and Methods

Subjects. Study participants were recruited at Bojonegoro Police Clinic and Bojonegoro Bhayangkara Hospital. The study was conducted from March to April 2022. The eligibility criteria for the study subjects included prediabetic patients, aged 18–58 years, and had mobile phones with camera features for diet monitoring. According to the American Diabetes Association's (ADA 2022) recommendations, prediabetic criteria were defined as fasting plasma glucose of 100–126 mg/dl, 2 h post-challenge blood glucose of 140–199 mg/dl, or HbA1c of 5.7–6.4%. We excluded subjects diagnosed with the conditions below, i.e., diabetes, pregnancy, malignancy, liver cirrhosis Child-Pugh B or C, infectious states, and had the glomerular filtration rate less than 60 ml/min/1.73 m^2. Subjects taking a steroid, anti-obesity, or blood glucose-lowering drug were also excluded from the study. The sample size was estimated using a formula with paired numerical data of more than one group which required a minimum of 22 subjects. A total of 26 study subjects participated in the present study. Written informed consent was obtained from all study subjects before attending the study.

Study design and protocols. The current study was a pretest-posttest randomized experimental design.

Study subjects were divided into three groups based on BMI categories (i.e., normal weight, overweight, and obese group), then assigned to control and intervention groups by randomization. The control group was asked to maintain their habitual diet of white rice, while the intervention group was instructed to replace their habitual diet of white rice with sorghum grain for seven consecutive days. We used white rice as a control since it is highly consumed as a staple food by the Indonesian population. Sorghum grain or white rice was consumed three times a day with a total intake per serving controlled by a dietician based on daily intake requirement. Participants handled the test meal preparation with guidance from the researcher's team. Food images captured during eating episodes were reported by each participant to the researcher's team for the dietary assessment. Study subjects were asked to not change their dietary habits during the intervention period, except for the asked instruction. All study subjects were given education about healthy lifestyles and also asked to implement the standard healthy lifestyles. The study was approved by the Health Research Ethics Committee of Dr. Soetomo General Hospital Surabaya Indonesia with recommendation number 52/EC/KEPK/FKUA/2022.

Anthropometric data and biochemical analysis. Clinical and anthropometric data (i.e., age, gender, history of smoking, body weight, body height, waist circumference, and blood pressure) were obtained from all study subjects. Body height and weight were examined to calculate body mass index [BMI=weight (kg)/height^2 (m^2)]. BMI was stratified into normal weight for BMI of 18.5–24.9 kg/m^2, overweight for BMI of 25–29.9 kg/m^2, and obesity for BMI of more than 30 kg/m^2 (NIH 1998). Waist circumference (WC) was measured at the midpoint between the last rib and the iliac crest using a measuring tape to the nearest 0.1 cm. WC ≥80 cm for women or WC ≥90 cm for men was adopted as the criteria to diagnose abdominal obesity (central obesity) based on IDF's recommendation for South Asia countries (Alberti et al. 2005). Overnight fasting blood samples were collected from all of the study subjects before the intervention period. Glycemic and lipid variables (i.e., fasting blood glucose, FBG; fasting insulin, total cholesterol, TC; high-density lipoprotein cholesterol, HDL-c; triglycerides, TG; and low-density lipoprotein cholesterol, LDL-c) were measured using standard laboratory techniques. Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) as a surrogate indicator of insulin resistance was calculated according to the formula: fasting insulin (microU/L) × fasting blood glucose (nmol/L)/22.5. HOMA-IR more than 2.5 was considered as a cutoff value to establish the insulin resistance condition (Singh et al. 2013). Non-high-density lipoprotein cholesterol (non-HDL-c) was obtained by subtracting HDL-c from TC. Diagnosis of dyslipidemia was based on the US National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III 2002) guidelines. Adiponectin was measured at the beginning and after the intervention period in both groups. Adiponectin concentration was measured as total adiponectin by ELISA kit (CAN-APN-5000, Diagnostics Biochem Canada Inc). Delta adiponectin in both groups was determined by subtracting adiponectin concentration post-intervention from the concentration pre-intervention.

Statistical analysis. Statistical analysis was conducted using SPSS 28.0 software. The results of the study were presented in tabular and box-plot forms. Continuous variables were reported as mean and standard deviation for normally distributed data. Continuous variables with asymmetrically distributed data were reported as median and interquartile range. Categorical variables were reported as frequency and percentage. The normality of the data was assessed using Shapiro-Wilk test. Comparison of clinical characteristics and biochemical parameters between the intervention and control groups were assessed using independent sample t test for normally distributed data, Mann Whitney U test for asymmetrically distributed data, and Chi-square test for categorical variables. The average adiponectin concentration at the beginning and the end of the intervention were compared using paired t-test for normally distributed data or Wilcoxon signed-rank test for skewed distributed data. The difference in adiponectin concentration between BMI categories was assessed using Kruskal-Wallis test. P value<0.05 was considered statistically significant.

Results

A total of 26 participants completed the study. There were 13 subjects in the control group and 13 subjects in the sorghum intervention group. There were no significant differences in clinical and anthropometric parameters in the groups, except a higher mean of age in the intervention group as shown in Table 1. Laboratory parameters of glycemic variables, lipid profiles, and adiponectin concentrations in baseline showed no significant difference in both groups, except the significantly higher LDL-c concentration in the intervention than the

Table 1
Baseline characteristics of the study population

Variables	Control group (n=13)	Intervention group (n=13)	p-value
Clinical variables			
Age (years)	34±8	40±5	0.044[a]
Gender (Male %)	8 (61.5%)	5 (38.5%)	0.239[b]
Active smoker (%)	4 (36.8%)	2 (15.4%)	0.645[b]
Presence of dyslipidemia (%)	10 (76.9%)	11 (84.6%)	1.000[b]
Systolic pressure (mmHg)	121±15	123±12	0.729[a]
Diastolic pressure (mmHg)	80 (76–84)	80 (79–88)	0.362[c]
Anthropometric variables			
Waist circumference (cm)	94 (78.5–99.5)	94 (88–95.5)	0.898[c]
Central obesity (%)	9 (69.2%)	11 (84.6%)	0.645[b]
BMI (kg/m^2)	27.4±4.0	28.3±4.6	0.603[a]
Normal weight (%)	3 (23.1%)	3 (23.1%)	
Overweight (%)	6 (46.2%)	5 (38.5%)	0.904[b]
Obesity (%)	4 (30.8%)	5 (38.5%)	
Biochemical variables			
Fasting plasma glucose (mg/dL)	102 (100-108)	104 (100-110)	0.579[c]
Fasting insulin (µU/ml)	26.46±9.36	26.93±7.56	0.890[a]
HOMA-IR	6.92±2.55	7.10±2.17	0.851[a]
Cholesterol total (mg/dl)	188±24	203±32	0.187[a]
Triglycerides (mg/dl)	249 (78–392)	147 (102–244)	0.369[c]
LDL-c (mg/dl)	114 (88–132)	141 (124–169)	0.013[c]
HDL-c (mg/dl)	44±8	49±8	0.170[a]
Non-HDL-c (mg/dl)	143±23	154±32	0.329[a]
Adiponectin (µg/ml)	6.64 (5.62–9.49)	6.50 (4.90–8.78)	0.397[c]
Daily consumption of test meal			
Total calories (kcal)	970.71±44.29	961.45±82.24	0.732[a]
Carbohydrate (g)	132.35 (72.80–139.60)	125.00 (98.00–148.60)	0.574[c]
Protein (g)	44.58±6.53	46.37±9.25	0.584[a]
Fat (g)	36.33±5.09	34.41±5.98	0.397[a]
Cholesterol (g)	68.65 (46.0-301.8)	103.60 (18.40-556)	0.810[c]
Fiber (g)	9.40±2.04	9.48±1.97	0.850[a]

Abbreviations: BMI – body mass index; HOMA-IR – Homeostasis Model Assessment for Insulin Resistance; HDL-c – high-density lipoprotein cholesterol; LDL-c – low-density lipoprotein cholesterol. Data are presented as mean ± standard deviations or median (interquartile range). [a]Independent sample t-test; [b]Chi-square; [c]Mann Whitney U test.

control group (p=0.013). Compositions of test meals in both groups had similar calories, macronutrients, and fiber contents as is reported in Table 1. Adiponectin levels after the intervention period in both groups decreased significantly from the baseline as presented in Figure 1. The change of decreasing adiponectin level is greater in the control group than in the sorghum intervention group, but statistically insignificant (p=0.522). Adiponectin concentrations of the control and sorghum group after the intervention period also decreased from the baseline in all BMI groups, but only statistically significant was in the overweight control group (p=0.028) as shown in Table 2. The average of decreasing adiponectin level in the sorghum group was greater in the obese group than other BMI groups, but no statistical significancy

Table 2
Comparison of plasma adiponectin concentrations according to BMI categories

BMI categories	Control Group			[1]p-value	Intervention Group			[1]p-value	[2]p-value
	Plasma Adiponectin Concentration (µg/ml)				Plasma Adiponectin Concentration (µg/ml)				
	Baseline	Endpoint	Delta		Baseline	Endpoint	Delta		
Normal weight	16.81±16.37	9.59±7.18	−7.22±9.70	0.184	7.11±0.76	4.54±0.86	−2.57±1.52	0.441	0.495
Overweight	6.38 (5.68–7.25)	3.38 (3.09–5.24)	−2.40±1.33	0.028	4.70 (4.16–16.63)	3.92 (2.90–11.83)	−2.57±8.04	0.345	0.958
Obesity	10.89±7.44	4.40±1.60	−2.87 (−14.6 – −2.03)	0.752	7.90±2.63	4.27±1.08	−3.53 (−5.59 – −1.72)	0.387	1.000
[3]p-value	0.562	0.597	0.825		0.267	0.983	0.470		

Abbreviations: BMI – body mass index. Data are presented as mean ± standard deviation or median (interquartile range). [1]p – comparison between adiponectin concentrations in the baseline and endpoint within the group; [2]p – comparison between delta adiponectin of control and intervention groups within BMI categories; [3]p – comparison of adiponectin concentrations among BMI categories within the group.

was found. There was no significant difference in adiponectin concentrations between BMI groups.

Discussion

Our study demonstrated that the median values of adiponectin level in both groups at the baseline were lower than the median of adiponectin level with the same BMI category in a previous large general population-based study. The study conducted by Nielsen et al. (2020) involving more than 30 000 Danish individuals has shown that the median plasma adiponectin level in the overweight group was 15.1 µg/ml, which is higher than in our study results. A previous meta-analysis study conducted by Lai et al. (2015) has reported that adiponectin level in prediabetic population is significantly lower than in healthy controls with the median range of adiponectin level in the overweight group within 2.78–12.90 µg/ml, which is consistent with our data. Plasma adiponectin level is known to be inversely associated with adiposity and decreased in obesity and insulin resistance conditions (Halleux et al. 2001). The median of HOMA-IR in the present study indicated that both groups had insulin resistance conditions. More than three-quarters of the study subjects were also classified into overweight and obese categories based on BMI stratification. Moreover, the average of our study subjects had abdominal obesity with the median values of waist circumference in both groups 94 cm. Those variables might have contributed to low adiponectin levels in our study.

The main purpose of our study was to examine the effect of dietary sorghum grain as a substitution for white rice for a week on plasma adiponectin levels in prediabetic patients. Adiponectin levels

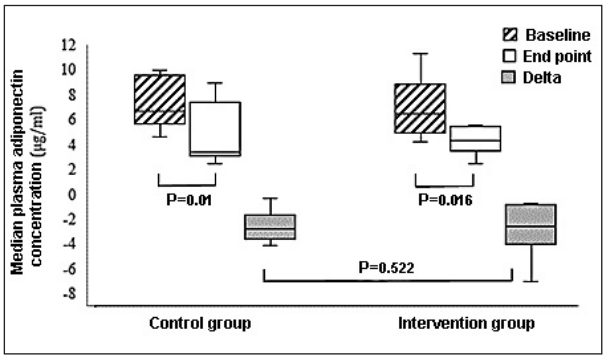

Figure 1. Plasma adiponectin concentrations of control and intervention groups evaluated at the baseline and endpoint. [a]Wilcoxon signed-rank test; [b]Mann Whitney U test.

after one week in white rice and sorghum groups decreased from the baseline in all BMI groups with a statistically significant difference only found in the overweight control group (p=0.028). The delta values of decreasing adiponectin levels were not significant in all groups. Our results suggested that sorghum consumption for a week did not differ from white rice in affecting the plasma adiponectin levels in the prediabetic patients and might be insufficient to delay the progression of decreased adiponectin levels in those populations. This result did not support the results of prior *in vitro* and *in vivo* animal studies that have reported the significant positive effect of sorghum extract on adiponectin protein expression in adipose tissue (Park et al. 2012; Lee et al. 2022). The previous studies have suggested that phenolic compounds in sorghum extract might induce over-expression of PPAR-γ and reduced TNF-α expression in adipose tissue that consequently increases adiponectin expression. Our study used sorghum

grain, which might have a lower phenolic concentration than sorghum extract. A previous *in vitro* study has revealed that the hypoglycemic ability of sorghum by inhibiting α-glucosidase and α-amylase activity was positively dependent on the concentration of phenolic content (Xiong et al. 2020). Other studies have also demonstrated that phenolic concentrations of sorghum were affected by the sorghum variety and the cooking process (Xiong et al. 2020; Xu et al. 2021). Further studies investigating sorghum phenolic extract from different varieties of sorghum on affecting adiponectin may need to be developed.

Sorghum primarily consists of starch with the component of resistant starch higher than other cereals (Taylor and Duodu 2023). Resistant starch is a carbohydrate that is resistant to digestion in the small intestine and fermented to short-chain fatty acids by the microbiota in the large intestine thus functioning like dietary fiber. A recent study has reported that resistant starch and fiber content in sorghum along with complexation to tannin that reduces the digestibility of these nutrients is associated with an increased satiety and reduced energy level that may have potential benefits for weight-loss management in obese patients (Simnadis et al. 2016). A randomized controlled study in overweight men has shown that extruded sorghum consumption along with a calorie-restricted diet for 8 weeks is significantly associated with a reduction of body fat compared to wheat control (Anunciacao et al. 2019). Correspondingly, previous studies have reported that weight loss, including a reduction in body fat, is associated with increasing circulating adiponectin concentration (Yang et al. 2001; Kopp et al. 2005). These studies have suggested that the increase of adiponectin level induced by weight loss may be associated with an improvement of risk factors, particularly, an increase in insulin sensitivity and reduction of inflammatory markers. It can be assumed that resistant starch, fiber content, and tannin in sorghum may also have the potential in increasing circulating adiponectin levels through weight-loss mechanisms. The interventional study by Ma et al. (2016) has revealed that long-term weight-loss diets for 2 years significantly increase plasma adiponectin levels and found that the increase of adiponectin was significantly associated with a significant reduction in body weight and waist circumference. Therefore, we proposed that longer sorghum consumption may be needed to produce the reduction of body weight that can be associated with the increased adiponectin level.

Sorghum has abundant sources of various phytochemical substances, e.g., anthocyanin. A previous study evaluating the effect of supplements containing anthocyanin-rich grape powder for four weeks in men with metabolic syndrome has reported a significant positive effect on circulating adiponectin levels in subjects without dyslipidemia, but not in those with dyslipidemia (Barona et al. 2012). This study has suggested that individuals with dyslipidemia may have increased the inflammation level, which may consequently be less responsive to dietary intervention. The prevalence of dyslipidemia in our study population is more than 75% in both groups with the highest medians of lipid profile components in the control group and the sorghum group were triglycerides and LDL-c levels, respectively. The majority of study subjects also met the criteria for either metabolically unhealthy overweight (MUOW) or metabolically unhealthy obesity (MUO) based on the criteria proposed by Liu et al. (2019) using diagnosis components of metabolic syndrome and insulin resistance. Most metabolic abnormalities found in our study population were insulin resistance, central obesity, and dyslipidemia. In comparison to metabolically healthy obesity (MHO), which is defined as individuals with BMI ≥30 kg/m^2 with the absence of any metabolic abnormalities (Mudjanarko 2022), MUOW and MUO have reported to have a higher risk for developing cardiovascular diseases (Wang et al 2021). A prior prospective cohort study analyzing 1739 adults has demonstrated that adherence to the Mediterranean dietary pattern did not reduce mortality among MUO phenotypes (Park et al. 2016). The study has suggested that MUO individuals might be less responsive to dietary alone because they are already metabolically overburdened. The majority of unhealthy metabolic conditions in our study subjects could explain the results of the present study. Park et al. (2016) have recommended that more intensive interventions are needed to reduce morbidity in those individuals.

Study limitations. This study has certain limitations. First, the sample size was relatively small. Either the test meal preparation or consumption was carried out in each participant's place with guidance from the researcher's team. Thus, it is a bit difficult for controlling the intake of the test meal or other additional calories even though there were food records and discussions during the trials. Our study also investigated the effect of sorghum consumption on adiponectin levels in a short period that might be insufficient to produce the favorable effect of sorghum on adiponectin. Nonetheless, this is the first study to evaluate the effect of sorghum consumption on adiponectin levels in the prediabetic population as

a key strength of the present study. Other studies to evaluate the effect of sorghum grain on adiponectin levels with different varieties of sorghum, other sorghum forms (e.g., sorghum extract, sorghum flour, extruded products, etc.), or different types of populations are needed to be developed. To better understand the specific sorghum component that affects adiponectin more studies are recommended. Further studies evaluating the effect of sorghum consumption on adiponectin levels in longer periods are also warranted.

Conclusion

Sorghum consumption for a week is not sufficient to increase adiponectin levels in the prediabetic patients. Insulin resistance, central obesity, and dyslipidemia may be the confounding variables that alter the favorable effect of sorghum on adiponectin levels. Either longer sorghum consumption or other interventions may be needed to increase the adiponectin levels in people with prediabetic conditions.

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Conflict of Interest: *The authors reported no conflict of interest.*

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