

Fructose Intake Related with Serum Uric Acid Level in Young Adults

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ABSTRACT

This study aimed to clarify the correlation of fructose intake with uric acid level and blood pressure in young adults. This study used a cross-sectional design, conducted in Padang, West Sumatera province of Indonesia in 2014. The subjects consist of 109 students of Medical Faculty of Andalas University, aged 18–23 years old, were randomly selected to participate. Data on fructose intake were obtained using food frequency questionnaire. Uric acid levels was determined by the enzymatic colorimetric method. Resting blood pressure was measured twice using a sphygmomanometer. Data were analyzed using Rank-Spearman correlation test. The median of fructose intake was 74.3 g (min 23.4–max 160.2). The median of systolic blood pressure was 117 mmHg (min 100–max 145) and median of diastolic blood pressure was 70 mmHg (min 60–max 90). The mean uric acid levels was 5.2 ± 1.56 mg/dl and 25% of the male subject had high uric acid levels. Fructose intake had no significant correlation with SBP ($r=0.026$; $p=0.851$) nor with DBP ($r=0.051$; $p=0.712$). However, there was a strong correlation between fructose intake with uric acid level ($r=0.660$; $p<0.001$). The study found that fructose intake shows a strong correlation with uric acid level but not with blood pressure in young adult.

Keywords: blood pressure, fructose intake, uric acid

INTRODUCTION

Overweight and obesity has been a health problems world wide and is the 5th leading cause of death in the world. World Health Organization states that 2.8 million people die/year due to overweight or obesity. In 2008 more than 1.4 billion adults aged 20 years and over suffered overweight and 10% of men and 14% of women in the world suffered from obesity (WHO 2012).

According to the Indonesian Basic Health Research 2010 report, the prevalence of Indonesian people age >18 years who suffered from overweight and obesity was 21.7% and was higher in women (26.9%) compared to men (16.3%) (Kotsis *et al.* 2010). This prevalence is higher than the data in 2007, where it was only 19.1% (MoH 2007). While in West Sumatra the prevalence of obesity is 20% in 2018 (MoH 2018).

Obesity causes various metabolic disorders, including disorders of uric acid metabolism. Study has found that serum uric acid level of people with obesity was 10 times higher than people with normal weight. This is caused by the declined in acid clearance and

increase in uric acid production. (Alboqai *et al.* 2007). Hyperuricemia is caused by many factors, including excessive consumption of sweeteners (Gee *et al.* 2008). The most frequent type of sweeteners found in food are glucose and fructose form. In the last 20 years, fructose consumption has increased as much as 16% in the United States and 50% in Asia (Tappy & Kim 2010). One of the contributor for the increase in fructose based sweeteners intake is consumption of sweet beverages. In Indonesia, consumption of sweet beverages in adolescents and young adults is around 21-23% (Febriyani *et al.* 2012)

High fructose intake can affect the uric acid metabolism in the body. It is associated with the occurrence of hyperuricemia because fructose metabolism can increase uric acid formation (Tappy & Kim 2010). However, research have shown conflicting results. Some studies showed that high fructose intake on a hyper caloric diet causes an increase in serum uric acid levels (Wang *et al.* 2012). While other reported that high fructose intake was not associated with an increased risk of hyperuricemia in adults (Sun *et al.* 2010). Likewise, the research in Florida states found that there was no correlation between

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fructose consumption and uric acid levels (Angelopoulos *et al.* 2015).

In addition, high fructose intake increases sodium reabsorption in the small intestine, causing an increase in fluid volume which will ultimately increase preload and cardiac output (Desmawati 2017). This increase in preload and cardiac output will cause an increase in blood pressure. However, the results of research on the relationship of fructose with blood pressure have also not been consistent. Research on adolescents in Taiwan stated that there was a significant relationship between fructose intake and SBP but not with DBP (Lin *et al.* 2013). While other studies found no significant relationship between fructose intake and blood pressure (Angelopoulos *et al.* 2015). The purpose of this study was to clarify the correlation between fructose intake with serum uric acid levels and blood pressure in young adults.

METHODS

Design, location, and time

This study used a cross-sectional design, conducted at the Medical Faculty of Andalas University, West Sumatera Province of Indonesia from February to October 2014.

Sampling

The sample size was calculated using the Lemeshow formula with an estimated proportion of 0.5 and the minimum sample size was 97 subjects. Then, 120 subjects were taken to anticipate a drop out subjects (incomplete data). The subjects were medical students from Andalas University aged 18-23 years who met the inclusion criteria. The inclusion criteria in this study were ages 18-23 years, had a normal BMI and overweight ($BMI \geq 18.5 \text{ kg/m}^2$) and were willing to be the subject of research by signing informed consent. While students who suffer from Diabetes Mellitus (diagnosis was based on review), have undergone extensive gastrointestinal surgery (doctor's information), and fever were excluded from the study. A total of 120 students were selected by simple random sampling and after screened, 115 students had met the inclusion criteria. However only 110 students came for blood collection and 1 subject was excluded from the study because of incomplete anthropometric data, a total of 109 subjects were included in statistical analysis.

Data collection

The anthropometric examination to determine nutritional status, blood pressure, and laboratory examinations were performed on 110 subjects. Interviews to determine fructose intake were carried out by trained enumerators using semi quantitative-food frequency questionnaire (SQ-FFQ), then analysed using the Nutri Survey. As much as 3 ml of venous blood was taken from the fossa cubiti by a trained laboratory officer from Prodia Padang Laboratory to examine uric acid levels. Examination of uric acid levels was carried out by the enzymatic colorimetric method. Blood pressure was measured twice using a sphygmomanometer, in a sitting position after the subject has rested for 10 minutes.

Data analysis

All data were analyzed using the SPSS software (version 22.0 for Windows, IBM Corporate, New York, Armonk) and to see the correlation of fructose intake with blood pressure and the uric acid level was performed Rank-Spearman correlation test with significance <0.05 .

RESULTS AND DISCUSSION

The research subjects were students aged 18-23 years, with the median age of 20.5 years. In this study, the proportion of female subjects (55.05%) was slightly higher than the male (44.95%) 82,6% subjects have normal nutritional status.

Fructose intakes of research subjects was obtained from interviews using SQ-FFQ, with the average value of fructose intakes in the study subjects was 74.3 g/day (min 23.4-max 160.2). This amount is higher than the recommended amount of 60 g/day (Desmawati 2017). High intake of fructose continuously for a long time can cause various health problems. Research conducted by Bray *et al.* (2004) states that fructose consumption over the past 10 to 20 years

Table 1. Distribution of fructose intake, blood pressure and uric acid levels of young adults

Variable	Median	Min	Max
Fructose intake (g)	74.3	23.4	160.2
SBP	117	100	145
DBP	70	60	90

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure

has been linked to a rise in obesity and metabolic disorders. Besides that, dietary fructose has been implicated in risk factors for Cardiovascular Disease (CVD), namely by increasing plasma Triglycerides (TG) and Very Low Density Lipid Triglycerides (VLDL-TG). These two substances are increased following the ingestion of large quantities of fructose. Insulin and leptin resistance can also occur due to chronic consumption of fructose (Rizkalla 2010).

The median SBP of the subjects was 117 mmHg (min 100–max 145) and the median DBP was 70 mmHg (min 60–max 90) (Table 1). The mean blood pressure of study subjects was within the normal range, but there were some people who suffered from hypertension. Hypertension was known as high or raised blood pressure with an increase in SBP ≥ 140 mmHg and or an increase in DBP ≥ 90 mmHg (Chobanian *et al.* 2003). But, the American College of Cardiology/American Heart Association (ACC/AHA) 2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults has provided updated BP thresholds for defining hypertension. ACC/AHA defined hypertension as systolic BP ≥ 130 mmHg or diastolic BP ≥ 80 mmHg (Doran *et al.* 2018). At present, the incidence of hypertension occurs at a younger age. It can be caused by various things, including unhealthy lifestyles, including high consumption of fructose (Rizkalla 2010). In this study found several subjects suffering from hypertension even though they are still young adults. Fructose intake in the most subjects were higher than the recommended amount.

Examination of serum uric acid levels was carried out after fasting for 8-12 hours. The average uric acid level of the subjects was 5.2 (± 1.56) mg/dl. Most of the subjects's uric acid

levels were within the normal limits, but there was a high uric acid level in 24.49% of the male subjects (Table 2). Previous studies conducted on ethnic Minangkabau adult males in Padang city found that hyperuricemia occurred in 21% of study subjects. That result is higher than the current research results, this is due to differences in age of the subjects. Previous studies conducted at the age range of 40-50 years, while this study was conducted in young adults. Purine and fructose intake are also related to uric acid levels, but in this study purine intake was not examined (Desmawati 2019)

In this study, there was a strong correlation between fructose intake and serum uric acid levels in the subjects. This result is supported by other studies. The National Health and Nutrition Examination Survey III (NHANES III), a health and nutritional status assessment program of adults and children in the United States, shows that fructose-rich drinks, both artificial (soft drinks) and natural (orange juice) are associated with increase in serum uric acid levels (Choi *et al.* 2008). The NHANES data from 4867 adolescents aged 12–18 years in 1999–2004 showed that consumption of artificial sweeteners (including fructose) was associated with increased in blood pressure and uric acid levels and the relationship was not influenced by gender and obesity (Nguyen *et al.* 2009). However, other study found that the positive association between fructose consumption and the increase in serum uric acid levels was more consistent in men (Choi & Curhan 2008). The pathophysiology is that fructose induces uric acid production by increasing the degradation of ATP to AMP, which is a precursor of gout. Which then accelerates the synthesis of de novo purine and potentiate the production of uric acid (Rho *et al.* 2011).

Table 2. Distribution of uric acid levels of young adults by sex

Gender	Normal uric acid level		High uric acid level		Total
	n	%	n	%	
Male	37	75.51	12	24.49	49
Female	55	91.67	5	8.33	60
Total	92		17		109

Table 3. Correlation of fructose intake with blood pressure and uric acid levels of young adults

Variable	SBP		DBP		Uric acid levels	
	r	p	r	p	r	p
Fructose intake	0.026	0.851	0.051	0.712	0.660	0.001*

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; r: correlation coefficient; *Rank-Spearman correlation test significant at $p < 0.05$

A high fructose diet can increase the absorption of salt in jejunum and thus water absorption. Increased extracellular fluid volume in animals which was given fructose will cause a decreased in renin expression in the kidneys by 45% and a significant increase in blood pressure. Research on rats fed with high fructose diet (60% fructose) compared to controls (60% carbohydrate), proved that hypertension occurred after the administration of a high-fructose diet for 14 days. Conversely, in conditioned rats without Glut5, there was a failure of fructose absorption accompanied by failure of other nutrient absorption which caused severe hypotension followed by death within 7–10 days later. This proves that fructose can induce blood pressure through increased absorption of salt in the small intestine. This effect will be more pronounced if a high intake of fructose is accompanied by a high intake of salt (Barone *et al.* 2009). Other studies show that there is an increase of SBP in the group of rats given a high fructose diet start from the second week (Nyby *et al.* 2007).

In a randomized cross over study of 15 young adults aged 21–33 years old, Brown *et al.* (2008) found that there was a significant increase in blood pressure after consuming fructose in the subjects compared with consumption of water and glucose. In the group given fructose, there was also an increase in heart rate. This is probably mediated by an increase in cardiac output without compensatory peripheral vasodilatation.

In addition, a Randomized Controlled Trial (RCT) in adult men showed that daily administration of 200 g fructose for two weeks increases the ambulatory blood pressure 7 ± 2 mmHg for SBP ($P<0.004$) and 5 ± 2 mmHg for DBP ($P<0.007$). However, there was a significant difference in the daily blood pressure of subjects treated with allopurinol compared to the control group. Changes in DBP in the control group without allopurinol was 5.5 ± 1.8 (7.1%), was significantly greater than changes in blood pressure in the allopurinol group which was 0.5 ± 0.8 (0.7%) with $p<0.04$. However, there were no significant differences in changes in the 24-hour ambulatory blood pressure or nocturnal blood pressure between the two groups. The research proves that gout has a large effect on the pathophysiology of increasing blood pressure caused by increase in fructose intake (Perez-Poso *et al.* 2010).

The relationship between sugar intake and blood pressure in humans was also reported in NHANES 2003–2006 cross sectional study.

This study included 4528 adults aged >18 years without hypertension history. The results of this study indicate that the average fructose intake of subjects was 74 g/day, after being controlled by demographics, physical activity, total calorie intake, and other confounders such as salt, alcohol, and total carbohydrate intake. This amount is equivalent to 2.5 servings of soft drinks/day. The study concluded that fructose intake is independently and significantly related to blood pressure in adults without a history of hypertension (Jalal *et al.* 2010).

The present study, however, found that although the fructose intake was higher than recommended there was no significant correlation between the fructose intakes with blood pressure ($p>0.05$). The results of this study are in line with previous research. The cohort research of the Framingham Heart Study (1998-2001) on 6039 subjects found that 35% of the subjects consumed soft drinks >1 serving/day (12 oz. or 360 ml) and there were no significant differences in individual blood pressure of subjects consuming soft drinks <1 serving and >1 serving/day (Dhingra *et al.* 2007). NHANES research in 1999-2006 involving 25,506 people aged 12-18 years also reported the same result that there was no significant relationship between the intake of fructose and non-fructose with an increase in blood pressure (Sun *et al.* 2010). Thus the findings that Fructose intake did not correlate with blood pressure as shown in this study probably because the study subjects were young, thus the hemodynamic controls were still good.

CONCLUSION

The study found significant correlation between fructose intake and serum uric acid but not with blood pressure in young adults. It is recommended that subjects lower their intake of fructose containing foods and beverages due to the increasing of uric acid levels. Therefore future longitudinal study of this cohort or a cross sectional study of wider age range will help further clarification on the correlation of fructose consumption and blood pressure.

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