

**Correlation between Fructose Consumption Habits and Insulin Resistance with TyG Index Biomarkers Manifesting Metabolic Syndrome at the Elderly Monjok Integrated Services Post (Posyandu)**

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**ABSTRACT**

**Aims:** This study aims to prove the relationship between the habit of consuming food and/or drinks containing fructose and the occurrence of insulin resistance which manifests as metabolic syndrome in subjects at the Elderly Monjok Integrated Service Post (Posyandu), Mataram City, Indonesia.

**Study design:** Observational study with a cross-sectional design

**Place and Duration of Study:** Sample: Elderly Monjok Integrated Service Post (Posyandu), Mataram City, Indonesia from May to July 2022.

**Methodology:** The study subjects were 48 people (10 men, 38 women, age range 45-90 years old). Fructose intake was collected using the *24 hours food recall* method and assessed using *the nutrisurvey software*. Insulin Resistance is determined by the *TyG Index* method. Metabolic Syndrome is determined based on the parameter of the *National Cholesterol Education Program Adult Treatment Panel III* (NCEP ATP III).

**Results:** The study results showed that 52.1% of the subjects at the Elderly Monjok Integrated Service Post (Posyandu) Mataram city had insulin resistance and 62.5% had metabolic syndrome. The *Chi-Square* test showed that there was a significant relationship between fructose consumption habits and the occurrence of insulin resistance ( $P=0.000$ ) and metabolic syndrome ( $P=0.001$ ).

**Conclusion:** This study proves that there is a significant relationship between fructose consumption habits and the occurrence of insulin resistance which manifests as metabolic syndrome, on the subjects at the Elderly Monjok Integrated Service Post (Posyandu), Mataram City, Indonesia.

*Keywords:* fructose consumption habits, metabolic syndrome, insulin resistance, *TyG index*

## 1. INTRODUCTION

Fructose is a monosaccharide type simple sugar. Based on the source, fructose is classified into natural sugars and artificial sweeteners. Fructose is a natural sugar when it

comes from fruits, vegetables or honey. Meanwhile, fructose as an artificial sweetener is usually found in the form of HFCS which is often used in prepared food/beverages, for example soft drinks, cookies, syrup, or cakes [1,2]. The mechanism of insulin resistance and the role of fructose in metabolic diseases begins when the consumed fructose undergoes a metabolic process. Fructose that has been catalyzed by fructokinase becomes fructose-1-phosphate, which is further broken down by aldolase B (AldoB) into glyceraldehyde and dihydroxyacetone phosphate. Glyceraldehyde provides the carbon chains used in the production of pyruvate, which then goes to the mitochondrial matrix to be reduced to Acetyl-CoA. Acetyl-CoA enters the Krebs cycle and produces citrate which is then released from the mitochondria into the cytoplasm to be converted to malonyl-CoA by the enzyme acetyl-CoA carboxylase (ACC). Excess malonyl-CoA in the cytoplasm inhibits the activity of the protein Carnitin Palmitoyl Transferase 1 (CPT-1), thus blocking the transport of lipids to mitochondria, and stopping  $\beta$ -oxidation. Malonyl-CoA is then converted to acyl-CoA by fatty acyl-CoA synthase (FAS) enzyme. The ACC and FAS enzymes are regulated by the activation of sterol regulatory element-binding protein-1c (SREBP1c) and carbohydrate responsive element-binding protein (ChREBP). Acyl-CoA then forms triglyceride molecules which accumulate in hepatocytes, causing non-alcoholic fatty liver disease (NAFLD). On the other hand, acyl-CoA can also bind to apolipoprotein (ApoB) to produce very low density lipoprotein (VLDL). In addition, acyl-CoA can also be converted into diacylglycerol (DAG) by diacylglycerol acyltransferase. Diacylglycerol (DAG) will then activate protein kinase C epsilon (PKC $\epsilon$ ), which in turn activates protein c-jun-N terminal kinase-1 (JNK1). This protein causes hepatic insulin resistance through IRS-1 phosphorylation at Serine307 residue (IRS-1Ser307). The mechanism of insulin resistance contributes to gluconeogenesis which causes hyperglycemia. In addition, acyl-CoA can also bind to apolipoprotein (ApoB) to produce VLDL and release free fatty acids. Ultimately fructose can cause: adipose tissue hypertrophy, insulin resistance, inhibition of insulin secretion, and TG accumulation in peripheral tissues [3].

Metabolic syndrome is an accumulation of several disorders or conditions that together can increase the risk of developing metabolic diseases such as cardiovascular, atherosclerotic, and diabetes mellitus [4]. The risk factor for metabolic syndrome is insulin resistance, which is the inability of insulin to optimally stimulate the transport of glucose into the body's cells (hyperinsulinemia or glucose tolerance) [5]. One of the measurements to predict insulin resistance can be done using the Triglyceride and glucose index (TyG index) method [6]. A person is said to have metabolic syndrome if there are three out of five metabolic abnormalities, namely waist circumference > 102 cm (men) or > 88cm (women); triglyceride level > 150 mg/dL; High Density Lipoprotein (HDL) cholesterol < 40 mg/dL (men) or < 50 mg/dL (women); fasting blood glucose level > 100 mg/dL, systolic blood pressure > 130 mmHg and diastolic > 85 mmHg [7,8,9]. Globally, it is estimated that 12-37% of the Asian population and 12-26% of the European population suffer from the metabolic syndrome. Meanwhile, the metabolic syndrome in Indonesia has a prevalence of 28% in men and 46% in women with the most prominent components being hypertension by 60% and hyperglycemia by 51% [9]. Data from the NTB Provincial Health Office for 2020, shows that the incidence of diseases which are parameters for metabolic syndrome such as hypertension is 7.19% close to the national figure of 8.36%; diabetes mellitus 1.2% approaching the national figure of 1.5%; while the RISKESDAS NTB 2018 data shows that central obesity (15.71%) and the incidence rate in Mataram City is the highest (21.39%) compared to other areas in the NTB Province [10,11]. Metabolic syndrome causes increased morbidity, mortality and disability so that it can reduce a person's quality of life and also have an impact on the high economic level of medical expenses. One of the risk factors that trigger the occurrence of metabolic syndrome is the wrong pattern of food and drink consumption among the public. Data from the Data and Information Center of Health Ministry in 2018 shows that 95% of Indonesian people do not consume fruits and vegetables. Currently, most people are used to consuming instant products that contain high

fructose in the form of high fructose corn syrup (HFCS), which triggers hypertriglyceridemia, hyperuricemia, increased LDL and decreased HDL, hypertension, and insulin resistance [12-17]. This is evidenced from the results of the Susenas March 2018 that 49.51% of the average percentage per capita expenditure per month is used to meet food needs. From this percentage the highest expenditure (16.82%) was spent on ready-made (instant) food and drinks [18]. Laura et al. 2008 stated that the recommended limit for fructose consumption is 25-40 grams/day [19]. Previous research showed that giving rats 10-21% fructose for >3 weeks induced an increase in body weight, systolic blood pressure, blood glucose, insulin, and triglycerides [20]. Departing from this problem, a study was conducted to find the relationship between consumption habits of foods and/or drinks containing fructose and the occurrence of metabolic syndrome which was determined based on blood pressure, central obesity, fasting triglyceride levels, fasting blood glucose levels, HDL, and insulin resistance. Identification of insulin resistance in this study used the TyG index which is relatively cheap, easy, available in almost all health facilities. When compared to HOMA-IR the Tyg index results are still accurate. In addition, HOMA-IR cannot be performed in all laboratories in health facilities because the parameter measured is insulin.

## 2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

This research is an observational study with a cross-sectional design using 48 subjects, from May to July 2022. Subjects were selected by consecutive sampling from Elderly Monjok Integrated Service Post (Posyandu), Mataram City, Indonesia with inclusion criteria, namely: subjects as participants in Elderly Monjok Integrated Service Post (Posyandu) aged 45-90 years, compos mentis, able to communicate properly, fill in informed consent, and domiciled in Mataram when the research took place. Exclusion criteria are: if the subject experiences a decrease in health status and has severe disease disorders.

The data analyzed was taken from primary data including food/foodstuff/beverage consumption data, collected by the 24-hour food recall method once on weekdays by nutritionists and researchers. Fasting triglyceride data and fasting blood sugar levels were measured using the Point of Care Testing (POCT) method; while HDL levels were measured by laboratory tests by health analysts. Secondary data including weight, height, waist circumference, and blood pressure were obtained from Integrated Service Post (Posyandu) staff during Posyandu activities based on the parameters of the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III).

## 3. RESULTS AND DISCUSSION

The subjects obtained in this study totaled 52 people, and 2 people were excluded because they experienced a decrease in health status and 2 people were not willing to carry out laboratory tests. The number of subjects dropping out was 4 people, so that the subjects participating in this study were 48 people with the characteristics presented in Table 1.

**Tabel 1. Subjects Characteristics at the Elderly Monjok Integrated Service Post (Posyandu)**

Characteristic	45-90 years old
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		n	%
N		48	100
Age	45-54 years old	14	29.2
	55-65 years old	17	35.4
	66-74 years old	7	14.6
	75-90 years old	10	20.8
Gender	Male	10	20.8
	Female	38	79.2
Marital Status	Married	32	66.7
	Death divorced	16	33.3
Religion	Islam	46	95.8
	Hindu	1	2.10
	Christian	1	2.10
Education	No school	2	4.20
	SD	13	27.1
	SMP	12	25.0
	SMA	14	29.2
	>SMA	7	14.6
Job	Housewife	29	60.4
	Retired	6	12.5
	Freelance worker	4	8.3
	Entrepreneur	5	10.4
	Craftsman	1	2.1
	Driver	1	2.1
	PNS Lecturer	1	2.1
Physical Activity	Mild		
	Moderate	11	22.9
	Severe	26	54.2
Medical History		11	22.9
	None		
	Hypertension	22	45.8
	Diabetes	5	10.4
	Hypertension & diabetes	2	4.20
Central Obesity	Other or do not know	2	4.20
	Yes	17	35.4
	No	28	58.3
IMT		20	41.7
	Underweight	2	4.20
	Normal Weight	19	39.6
	Excess Weight	10	20.8
	Obesity I	11	22.9
	Obesity II	6	12.5

*SD elementary school; SMP junior high school; SMA senior high school; IMT body mass index; BB weight.*

Table 2 shows the distribution of metabolic syndrome parameter examination values in subjects at the Elderly Monjok Integrated Service Post (Posyandu).

**Table 2. Distribution of metabolic syndrome parameter examination values in subjects at the Elderly Monjok Integrated Service Post (Posyandu).**

Characteristics	45-90 years old	
	Median	Minimum-maximum
LP (cm)	97.50	75-110
TDS (mmHg)	132	100-200
TDD (mmHg)	85	57-100
HDL (mg/dL)	21	11-55
TGP (mg/dL)	135	72-312
GDP (mg/dL)	101	62-469
TyG index (cut-off)	4.76	4.38-5.57

*LP waist circumference; TDS systolic blood pressure; TDD diastolic blood pressure; HDL high-density lipoproteins; TGP fasting triglycerides; GDP fasting blood sugar.*

Table 3 shows the relationship between fructose consumption habits and the occurrence of insulin resistance, a non-parametric test (Chi-Square Test) because it is ordinal and nominal categorical data for more than two groups and not paired. The Chi-Square test shows a P-value of 0.000 which means that there is a significant relationship between the habit of consuming fructose and the occurrence of insulin resistance ( $P < .05$ ).

**Table 3. Relationship between fructose consumption habits and the occurrence of insulin resistance in subjects at the Elderly Monjok Integrated Service Post (Posyandu).**

Characteristics	45-90 years old		P-value
	n	%	
Fructose Consumption (%)			0.000***
Low <25 gr/hari	5	10.4	
Medium 25-40 gr/hari	19	39.6	
High >40 gr/hari	24	50.0	
Insulin Resistance (%)			0.000***
Yes	25	52.1	
No	23	47.9	

\*\*\*Chi-Square Test

Table 4 shows the relationship between fructose consumption habits and the occurrence of metabolic syndrome, non-parametric test (Chi-Square Test) because the data are ordinal and nominal categorical, more than two groups, and unpaired. The Chi-Square test shows a P-value of 0.001 which means that there is a significant relationship between fructose consumption habits and the occurrence of metabolic syndrome ( $P < .05$ ).

**Table 4 The relationship between fructose consumption habits and the occurrence of metabolic syndrome in subjects at the Elderly Monjok Integrated Service Post (Posyandu).**

45-90 years old			
Characteristics	n	%	P-value
Fructose Consumption (%)			0.001***
Low <25 gr/hari	5	10.4	
Medium 25-40 gr/hari	19	39.6	
High >40 gr/hari	24	50.0	
Metabolic Syndrome (%)			0.001***
Yes	30	62.5	
No	18	37.5	

**Table 5 The relationship between insulin resistance and the occurrence of metabolic syndrome in subjects at the Elderly Monjok Integrated Service Post (Posyandu).**

45-90 years old			
Characteristic	n	%	P-value
Insulin Resistance (%)			0.000**
Yes	25	52.1	
No	23	47.9	
Metabolic Syndrome (%)			0.000**
Yes	30	62.5	
No	18	37.5	

24 people or 50% of the subjects at the Elderly Monjok Integrated Service Post (Posyandu) had high fructose consumption habits (> 40 g/day) out of a total sample of 48 people. Based

on Table 3 regarding the relationship between fructose consumption habits and the occurrence of insulin resistance in subjects at the Elderly Monjok Integrated Service Post (Posyandu), it shows that there is a significant relationship between fructose consumption habits and the occurrence of insulin resistance. These results are supported by the research by Periera (2017) and Taskinen (2019) that fructose causes insulin resistance. According to Johnson (2009) there are 2 pathways that explain the mechanism by which fructose induces insulin resistance through [1,3,21]. The first pathway is de novo lipogenesis which produces DAG, which is further converted into triglycerides and VLDL. DAG also activates PKC which interferes with insulin signaling, thus triggering insulin resistance [21]. The second pathway of ATP depletion is due to fructose phosphorylation by the ketohexokinase enzyme, resulting in uric acid production which has a systemic effect, namely reducing NO which causes a decrease in glucose uptake by skeletal muscles. Another effect is a direct cellular effect on adipocytes, namely increasing oxidative stress and decreasing adiponectin. Ultimately, these two effects are what trigger Insulin Resistance [21].

Based on Table 4, regarding the relationship between fructose consumption habits and the occurrence of metabolic syndrome in subjects at the Elderly Monjok Integrated Service Post (Posyandu), it shows that there is a significant relationship between fructose consumption habits and the occurrence of metabolic syndrome. These results are supported by research by Johnson et al. (2009) who demonstrated the effect of fructose on various organs [21]. In the brain, fructose activates taste centers, addictive behavior, leptin resistance, and neurostimulants so that fructose consumed in the long term has the potential to increase calorie intake which results in the loss of the 'satiety' signal in the brain. This condition eventually leads to overweight and even obesity [21]. In the liver, fructose triggers the DNL pathway by increasing the formation of triglycerides and VLDL, resulting in the accumulation of fat in the liver and the formation of uric acid as the formation of excessive use of ATP during fructose phosphorylation which ultimately triggers insulin resistance. In blood vessels can cause inflammation and endothelial dysfunction. In the kidney it causes renal vasoconstriction, glomerular hypertension, kidney damage and inflammation. In adipocytes it induces oxidative stress, inflammation, and a decrease in adiponectin which causes a decrease in lipid oxidation resulting in lipid accumulation. This ultimately triggers the metabolic syndrome characterized by insulin resistance, hypertension, central obesity, dyslipidemia, fatty liver, inflammation, oxidative stress, and hyperuricemia [21].

Based on Table 5, regarding the relationship between insulin resistance and metabolic syndrome in subjects at the Elderly Monjok Integrated Service Post (Posyandu), the data shows that there is a significant relationship between insulin resistance and metabolic syndrome. This is in accordance with the statement put forward by Rohman (2007) that the mechanisms considered to be involved in the occurrence of the metabolic syndrome are insulin resistance and central obesity [22]. Also in line with research by Alberti (2009) which proved that insulin resistance is a component that influences the development of metabolic syndrome [23].

The strengths of this study are using a 24 hour food recall form questionnaire which is easy to use, does not take long, and does not require expensive equipment. To ensure that the subject is not under or over reported, food intake data collection is assisted by food photo books and trained nutritionists as well as interview questions that are asked twice to confirm the subject, so that if the answers given are consistent then it can be ensured that there is no under or over report.

Meanwhile, the limitation of this study is that the study design is cross-sectional so it cannot explain the causal relationship between fructose consumption habits and insulin resistance and metabolic syndrome, so cohort studies and randomized controlled trials are still needed to evaluate the relationship between fructose consumption with insulin resistance and metabolic syndrome. In addition, interviews using the 24-hour recall method for data collection on food intake in this study were only conducted at one time during Posyandu activities, namely on weekdays so that bias could occur.

#### 4. CONCLUSION

This study proves that there is a significant relationship between fructose consumption habits and the occurrence of insulin resistance which manifests as metabolic syndrome, in subjects at the Elderly Monjok Integrated Service Post (Posyandu), Mataram City, Indonesia.

#### ETHICAL APPROVAL (WHERE EVER APPLICABLE)

This research has obtained ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, University of Indonesia with Number KET 451/UN2.F1/ETIK/PPM.00.02/2022.

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