Original Article

EFFECT OF BREADFRUIT LEAF EXTRACT (ARTOCARPUS ALTILIS) ON CHANGES IN SGPT AND SGOT LEVELS TYPE 2 DIABETES MELLITUS PATIENTS

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Abstract

Type 2 Diabetes Mellitus (T2DM) is chronic hyperglycemia due to insulin resistance where there is an accumulation of intracellular glycogen in hepatocytes which causes an increase in glycogen synthesis. Supplementing natural ingredients with hepatoprotective and anti-free radical activity can neutralize ROS increase and regenerate pancreatic cells damaged by T2DM. This study aims to analyze the effect of breadfruit leaf extract on SPGT and SGOT levels in T2DM patients, as many as 39 research samples aged 36-65 years. Through experimental research with randomized controlled trial pre and post-test, this study found that there was a significant difference (p = 0.02) in respondents' SGOT levels between the control group and the intervention group who were given breadfruit leaf extract (decreased to 1.31 grams), yet there was no significant difference in respondents' SGPT levels between those groups (p=0.121). This study also found the importance of monitoring and evaluating medication adherence for T2DM patients.

Keywords: breadfruit leaf extract, SGOT, SGPT, liver enzymes, T2DM.

Introduction

The International Diabetes Federation (IDF) estimates that 463 million people aged 20–79 years in the world suffer from DM. In 2019, the prevalence of DM was 9.3% of the total world population at the same age. IDF identified 10 countries with the highest number of DM sufferers in the world, of which China, India, and the United States occupy the top three ranks, each with 116.4 million people, 77 million people, and 31 million people (P2PTM, 2020). Indonesia ranks 7th with several sufferers of 10.7 million people. In 2013, the prevalence of DM at the age of 15 years was 1.5% then increased in 2018 to 2% (Kemenkes RI, 2018). It was further explained that the prevalence of DM based on sex ranged from 1.78% in women and 1.21% in men. And based on age group, the highest prevalence is in the 55–64-year age group, which is 6.3%. The prevalence of DM in South Sulawesi Province is 1.7%, and in Bone City itself, the prevalence is 2.2%.

The increase in the incidence of DM is followed by an increase in the incidence of complications. Complications experienced by patients vary from physical, psychological, social, and economic complications. Physical complications arise in the form of eye damage, kidney damage, heart disease, high blood pressure, stroke, and even gangrene. DM disease can also affect the quality of life of sufferers, such as psychological health, physical function, and social roles. Quality of life is one of the main criteria for determining healthcare interventions such as morbidity, mortality, fertility, and disability (Meidikayanti & Wahyuni, 2017). Several studies on quality of

life have shown that of 89 respondents with T2DM, 59.6% had a moderate quality of life, 27.0% had a good quality of life and 13.5% had poor quality of life (Larasati, 2012). Another study found that 55.1% of 49 T2DM patients had poor quality of life (Pertiwi, 2013). Patients also said that when they found out they had T2DM, they could no longer work, as usual, especially those who had complications with other diseases.

Liver function tests that are often used are serum aminotransferase, alkaline phosphatase, albumin, and prothrombin time. People with T2DM have a higher incidence of abnormal liver function than people without diabetes. A mild increase in transaminase values chronically reflects the development of insulin resistance. In Indonesia, serum aminotransferases such as alanine aminotransferase (ALT) are referred to as serum glutamic-pyruvic transaminase (SGPT), and aspartate aminotransferase (AST) indicates the concentration of hepatic intracellular enzymes present in the bloodstream known as serum glutamic-oxaloacetic transaminase (SGOT) (Saputra, 2017). SPGT is an enzyme that is useful in the process of protein metabolism in the body, if the liver does not function properly, SPGT will be released into the blood so that its levels in the blood increase. SGOT is an enzyme found in several body parts such as the heart, liver, and bile ducts. If the levels are high, it could be a sign of impaired liver function or other organs (Saputra, 2017) and the impact of T2DM on the liver function that requires intervention.

Breadfruit leaves are known as neuralgia, analgesic, anti-inflammatory, antioxidant, hepatoprotective, anticancer, antimicrobial, antiviral, and antifungal and can also be a natural insecticide. Breadfruit has hepatoprotective activity due to its flavonoid, saponin, tannin, steroid, champerol, and polyphenol content (Sairam *et al*., 2016). Saponin compounds in breadfruit leaves can lower blood glucose by inhibiting glucose transport in the gastrointestinal tract and stimulating insulin secretion in pancreatic beta cells. Alkaloids can work by reducing gluconeogenesis so that glucose levels in the body and insulin requirements decrease (Tandi *et al*., 2017). Flavonoids that act as antioxidants can inhibit the formation of free radicals by neutralizing the increase in Reactive Oxygen Species (ROS) due to DM and can regenerate damaged pancreatic cells. This can lead to uncontrolled gluconeogenesis, glycogenolysis, and lipolysis in hyperglycemic DM patients.

A study that tested the hepatoprotection activity of the ethyl acetate fraction of breadfruit leaves (Artocarpus altilis) in male Wistar mice induced by CCL found that the ethyl acetate fraction of breadfruit leaves could suppress the increase in SGPT, SGOT, and ALP where the SGPT and SGOT values were close to normal. Then the study of the effect of toxicity on male Wistar mice induced by ethylene glycol found that breadfruit leaf extract had a hepatoprotective effect on the parameters of ALT, AST, and liver hypertrophy in test animals (Handayani, 2020). In addition, breadfruit leaf extract was also found to reduce fasting blood glucose in prediabetes patients, rectify cholesterol levels, both low- and high-density lipoproteins, and triglycerides, as well as reducing their systolic and diastolic blood pressure (Sitorus, 2021). Due to these interesting findings related to the effect of breadfruit leaf extract on improving liver function in T2DM patients, encourages researchers to examine the levels of SGPT and SGOT in T2DM patients.

Methods

The approach used in this study was an experimental randomized controlled trial, pre and post-test design for T2DM patients in the 'Puskesmas Biru', Bone Regency. The location of this study was chosen because the prevalence of T2DM was recorded as the highest in that regency, which was 526 cases as well as being the population in this study. Samples were determined using a purposive technique where patients were aged between 20-60 years and willing to consume breadfruit leaf extract for 21 days. Apart from that, patient who is violently ill and/or pregnant, are not used as respondents in this study. The number of samples in this study was 39 respondents divided into the control group (20) and the intervention group (19).

Respondents in the intervention group were given breadfruit leaf extract in the form of capsules and a control card to record the time of consumption. Monitoring is also carried out through the family to ensure that respondents consume the capsules. This study also used a questionnaire to see the respondents' understanding of DM and their compliance with taking DM drugs. Researchers collaborated with trained health workers to carry out blood sampling procedures before and after treatment. Glucose, SGPT, and SGOT levels from blood samples were

examined at Prodia's clinical laboratory. The data analysis technique in this study used the Kolmogorov-Smirnov test to test the normality of the data which was then carried out with the T-test or Wilcoxon test, T-independent test, and chi-square data on the respondents' glucose, SGPT, and SGOT levels, both before and after the intervention.

Results

Characteristics of respondents

Based on the age group, the majority of respondents are 46–55 years old, most of whom have higher education and high school education. Since most of the respondents are female, on average the respondents also work as housewives as well. The job status of the household heads of the respondents is mostly employees.

Table-1. Characteristics of subjects

Variables	**Control Group**		**Intervention Group**		***p-value**
	n	**%**	**n**	**%**	
Age (year)					
36 – 45	3	15,0	3	15,8	0.884
46 – 55	12	60,0	10	52,6	
56 – 65	5	31,6	6	31,6	
Gender					
Male	4	20,0	6	31,6	0,408
Female	16	80,0	13	68,3	
Education level					
Elementary School	2	10,0	4	21,1	
Yunior High School	4	20,0	4	21,1	0,407
Senior High School	9	45,0	4	21,1	
University	5	25,0	7	36,8	
Occupation					
Housewife	11	55,0	10	52,6	
Farmer	-	-	1	5,3	0,657
Retirement	-	-	1	5,3	
employment	7	35,0	6	31,6	
Businessman	2	10,0	1	5,3	

Variables	Control Group		Intervention Group		*p-value
	n	%	n	%	
Patriarch's occupation					
Housewife	-	-	1	5,3	0,163
Farmer	1	5,0	4	21,1	
Retirement	-	-	2	10,5	
employment	11	55,0	6	31,6	
Businessman	8	40,0	6	31,6	
DM diagnostic history (year)					
1	2	10,0	8	42,1	0.008
2	11	55,0	3	15,8	
3	6	30,0	3	15,8	
4	1	5,0	5	26,3	
Body Mass Index (BMI) [kg/m^2]					
Normal	9	45,0	8	42,1	0,664
Overweight	6	30,0	8	42,1	
Obesity	5	25,0	3	15,8	

**Chi-Square*

Source: Data processed, 2022

Research data distribution

Generally, respondents have normal levels of SGOT and SGPT, but most of the respondents have a low level of adherence to taking medication.

Table-2. Distribution level of SGOT, SPGT, and Medication adherence

Variables	Control group				*p*	Intervention group				*p*
	Pre-test		Post-test			Pre-test		Post-test		
	n	%	n	%		n	%	n	%	
SGOT										
Normal	14	70,0	15	75,0	0,705	13	68,4	15	78,9	0,527
High	6	30,0	5	25,0		6	31,6	4	21,1	

Variables	Control group					Intervention group				
	Pre-test		Post-test		*p*	Pre-test		Post-test		*p*
	n	%	n	%		n	%	n	%	
SGPT										
Normal	14	70,0	14	70,0	1,000	12	63,2	15	78,9	0,083
High	6	30,0	6	30,0		7	36,8	4	21,1	
Medication adherence										
Low	17	85,0	8	40,0		18	94,7	6	31,6	
Moderate	3	15,0	8	40,0	0,001	-	-	11	57,9	0,001
High	-	-	4	20,0		1	5,3	2	10,5	

Source: Data processed, 2022

Comparative Analysis

The results of statistical testing showed that there was no significant difference in the mean scores of the results of SGOT, SGPT, and respondents' medication adherence in the two groups, respectively for the results of the pre and post-test.

Tabel-3. Analysis of differences and changes in mean values

Variables		Pre-test *(mean ± SD)*	Post-test *(mean ± SD)*	*p-value*	Δ
SGOT	Control Group (n=20)	25,15 ± 25,55	26,85 ± 25,36	0,028*	1,70 ± 3,78
	Intervention Group (n=19)	21,36 ± 6,86	20,05 ± 6,63	0,021*	-1,31 ± 2,86
	p-value	0,125**	0,944**		**0,002****
SGPT	Control Group (n=20)	20,80 ± 9,00	20,50 ± 9,81	0,673*	-0,30 ± 3,62
	Intervention Group (n=19)	22,94 ± 9,29	20,10 ± 8,79	0,020*	-2,84 ± 5,01
	p-value	0,254**	0,899**		**0,121****
Medication adherence	Control Group (n=20)	3,72 ± 1,72	6,07 ± 1,41	0,000*	2,35 ± 1,09
	Intervention Group (n=19)	3,77 ± 1,87	6,01 ± 1,46	0,000*	2,23 ± 1,25
	p-value	0,977**	0,842**		**0,853****

**Wilcoxon*

***Mann-Whitney*

Source: Data processed, 2022

SGOT levels in the intervention group decreased (-1.31), while in the control group there was a change (1.70), and the results above (Table-3) also showed a significant difference in changes in (Δ) SGOT levels between the two groups. . The decrease in SGPT levels in the intervention group (-2.84) and in the control group (-0.30) did not show a significant difference in changes in (Δ) levels of SGPT both. Changes also occurred in medication adherence in the intervention group (0.23) whereas the control group experienced an increase (2.35). In addition, adherence to consuming breadfruit leaf extract capsules could not be analyzed because all respondents regularly consume them by looking at the remaining capsules on weekly evaluations. This is also due to the daily monitoring carried out to ensure that respondents consume the capsules.

Discussion

Increased oxidative stress or ROS can contribute to the development of DM and chronic oxidative stress results in insulin resistance and ultimately leads to T2DM (Islam *et al*., 2020). Some possibilities such as elevated levels of ALT, AST, and Gamma-glutamyl transferase (GGT) may reflect excess fat deposition in the liver, a condition known as Nonalcoholic Fatty Liver Disease (Nonalcoholic Fatty Liver Disease). NAFLD). NAFLD is thought to be involved with metabolic syndrome which refers to several cardiovascular risk factors associated with insulin resistance, hypertension, central obesity, dyslipidemia, and T2DM.

Insulin resistance is identified as an impaired biological response to insulin stimulation of target tissues, especially the liver, muscle, and adipose tissue. Insulin resistance interferes with the disposal of glucose so that glucose cannot be used by cells and gluconeogenesis occurs as compensation. The use of alanine and other amino acids as gluconeogenic substrates increases T2DM and the ALT-driven stimulation of gluconeogenesis from alanine can also directly increase hyperglycemia (Martino *et al*., 2022). The liver has a mechanism to inactivate ROS, but if the amount is excessive, oxidative stress occurs which will damage important biomolecules such as lipids, proteins, and DNA (Velu *et al*., 2016), as a result, the liver function will be disrupted so it requires exogenous antioxidants (Hidayah, 2015).

This study found as many as 68.4% of respondents in the intervention group had normal SGOT levels, which increased to 78.9% after treatment, as well as in the control group which increased by 5% over the previous (70%). In addition, as many as 63.2% of respondents in the intervention group who had normal SGPT levels increased to 78.9%, but in the control group, there was no change. Referring to this finding clarifies the hepatoprotective activity of breadfruit plants (Sairam *et al*., 2016) mainly because of its flavonoid compounds which are negatively related to Fatty Liver Index (FLI), SGOT, and SGPT (Mazidi *et al*., 2019), where the greater the flavonoid intake, the more favourable the liver biomarker profile. The way flavonoids work is by removing electrons from free hydroxy groups, which will form unreactive compounds such as flavonoid phenoxy radicals After preventing the production of pyruvate, alpha-ketoglutarate, and oxaloacetate, these two compounds inhibit hepatic gluconeogenesis and consequently inhibit the development of DM (Zareei *et al*., 2017). Other compounds, alkaloids also reduce gluconeogenesis so that insulin requirements decrease (Tandi *et al*., 2017) and saponins have been shown to have potential as alternative drugs in lowering blood glucose levels in DM patients by activating glycogen synthesis, suppressing disaccharide activity, modulating insulin signalling, regenerating insulin action, increasing insulin release from beta cells, inhibiting glucogenesis, inhibiting -glucosidase activity, and increasing insulin expression. glucose transporter-4 (GLUT4) (El Barky *et al*., 2017).

However, the findings of this study still need to be investigated further because many other factors may affect changes in SGOT and SGPT levels, such as lifestyle, physical activity, alcohol consumption, smoking, and so on that were not examined in this study. This study also found that respondents' medication adherence was low and could affect the results of the study due to the possibility of a difference in the time required for the compounds contained in the breadfruit leaf extract to exert their effect on SGOT and SGPT levels. SGPT activity has diurnal variations – the nadir is at 4:00, and the peak value is at 16:00 (Ruhl & Everhart, 2013) although SGPT is generally believed to be more specific to the liver, it is also found in muscles and kidneys. Its half-life is 47 ± 10 hours which is higher than SGOT (Vuppalanchi & Chalasani, 2011). The lack of medication adherence allows SGOT to be affected by the administration of breadfruit leaf extract compared to SGPT, so this study found a significant effect on SGOT levels but not on respondents' SGPT levels.

Conclusion

The average level of SGOT in the group given breadfruit leaf extract decreased by -1.31, on the contrary, there was an increase in SGOT levels by 1.70 in the group that was not given. The average SGPT level in the group given breadfruit leaf extract decreased by -2.84, as well as in the group that was not given it also decreased by -0.30. There was a difference in changes in SGOT levels after the intervention between the intervention group and the control group with a value (0.002≤0.05), but there was no significant difference (0.121≥0.05) in the levels of SGPT in the two groups after treatment.

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