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The effect of giving breadfulness leaf drink on *High Density Lipoprotein* (HDL) in type 2 diabetes mellitus

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ABSTRACT

Background: Diabetes is one of the leading causes of death and affects many people regardless of country, age group, and gender. According to Riskesdas data, the prevalence of diabetes mellitus is increasing every year, so efforts are needed to address this issue. Breadfruit leaves contain antioxidant compounds that can improve lipid dysfunction. This study aims to assess the effect of breadfruit leaf drink on *High Density Lipoprotein (*HDL) levels in diabetes mellitus cases.

Method: This study was a *quasi-experimental* study with a randomized *pretest-posttest* design with a control group. Two treatment groups were used: the intervention group and the control group. Total sample size was 40 people. The variable in this study was *High-Density Lipoprotein (*HDL). The intervention group was given breadfruit leaf drink with cinnamon and education, while the control group was only given education. The intervention was carried out for 30 days. Data were analysed using *the paired t-test* and *Wilcoxon Rank Test.*

Results: The results of HDL level analysis in the intervention group were 47,95 *pretest* and 5868 *posttest* (*p value* = 0,003), while in the control group they were 47,19 *pretest* and 52,24 *posttest* (*p value* = 0,013).

Conclusion: Breadfruit leaf and cinnamon drink was associated with increased HDL levels, but these changes were not significantly greater than those in the control group. The observed improvements may be partly due to lifestyle education or dietary modifications.

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KEYWORDS

Artocarpus altilis, lipid metabolism, glycemic control.

INTRODUCTION

Diabetes mellitus (DM) is a progressive metabolic disorder that develops on the basis of insulin resistance and decreased insulin secretion, which can lead to chronic hyperglycaemia[1]. Diabetes is one of the leading causes of increased mortality and disability worldwide, affecting many people regardless of country, age group, or gender[2]. The two most common types of diabetes are type 1 diabetes mellitus and type 2 diabetes mellitus[3]. Type 2 diabetes impairs weight loss in those with excess fat. The mechanisms underlying this common clinical finding are multifactorial. These factors include energy conservation due to improved blood glucose control and reduced glucosuria, and hyperinsulinemia commonly found in patients with type 2 diabetes mellitus[4].

Type 2 diabetes mellitus is a condition characterised by hyperglycaemia and metabolic disorders that interfere with the healing process of bone and skin tissue[5]. The causes of metabolic disorders in type 2 diabetes mellitus are attributed to various factors. Individuals with diabetes mellitus have a twofold higher risk of developing heart disease compared to those without diabetes mellitus[6].

Metabolic disorders associated with diabetes primarily affect tissues such as adipose tissue, skeletal muscle, and the liver due to insulin resistance[7]. Impaired insulin secretion and elevated blood glucose levels (hyperglycemia) are major risk factors for macrovascular complications in both diabetic and non-diabetic individuals. Insulin resistance occurs when the body experiences prolonged energy overload. Ectopic lipid accumulation in the liver and skeletal muscle triggers the activation of signaling pathways that inhibit insulin action. This leads to a decrease in the muscle's ability to take up glucose and a decrease in the process of glycogen formation in the liver[8].

One factor that plays a role in CHD in type 2 DM is dyslipidaemia. The most common dyslipidaemia found in type 2 DM is an increase in TG levels and a decrease in HDL levels (ZA et al., 2022). In people with DM, HDL often experiences dysfunction characterised by changes in lipid composition that interfere with its normal function. HDL dysfunction causes the accumulation of cholesterol-filled macrophages and increases atherosclerosis, which is a major risk factor for cardiovascular disease[9]. HDL acts in the body as an antiatherogenic, anti-inflammatory, antioxidant, and antithrombotic agent. One type of lipid profile is considered positive because HDL is able to transport bad cholesterol from the endothelium within blood vessels[10].

Herbal plants play a crucial role in the treatment of diabetes mellitus because they are known to have strong anti-diabetic properties without harmful side effects[11]. One plant that is often used by the community is the breadfruit plant. The breadfruit plant is widely used by the community as an herbal medicine because it is believed to cure various diseases[12]. Breadfruit leaves (Artocarpus altilis) are one of the traditional medicines that are widely known to the Indonesian people. Flavonoids, hydrocyanic acid, acetylcholine, tannins, riboflavin, saponins, phenols, quercetin, kaempferol, and potassium are the chemical compounds in breadfruit leaves that are effective as medicine for diseases such as kidney, heart, liver, enlarged spleen, diabetes, and cancer[13].

A study aimed at determining the effectiveness of breadfruit leaves in lowering blood sugar levels in type 2 diabetic rats[14]. Ethanol extract of breadfruit leaves has the ability to lower blood sugar or antihyperglycaemic activity. At a dose of 400 mg/kgBW, blood sugar levels decreased more rapidly and significantly. A similar study[15] suggested that breadfruit leaves have an impact on pancreatic repair. Administration of 400 mg/kg of breadfruit leaf extract has the potential to reduce pancreatic damage. This protection is due to the antioxidant activity of breadfruit leaves, which can promote better insulin secretion.

Every year, the prevalence of diabetes mellitus continues to increase based on data presented by Riskesdas, so efforts or measures are needed to address this problem. Based on this description, the researchers were interested in conducting further research to determine the effect of breadfruit leaf drink on HDL in patients with diabetes mellitus.

MATERIALS AND METHODS

Research Design

This study was a quasi-experimental study with a randomized pretest-posttest design with a control group. Two treatment groups were used: the intervention group and the control group. HDL levels were first measured, followed by the treatment for 30 days. After 30 days, HDL levels were remeasured in both groups. HDL levels were measured by drawing venous blood from the Kimia Farma Laboratory using a Roche C303 instrument.

This study also used a Single Blind design where participants did not know whether they were in the "treatment group" or the "control group". The beverage composition consisted of 2 grams of dried breadfruit leaves and 1 gram of cinnamon powder, with the preparation process following herbal drink preparation method described by Zainuddinnur[16]. The intervention involved providing the sample with a herbal tea drink, along with a control card, which was filled out upon consumption. The drink was consumed once daily by brewing it with warm water approximately four hours after taking diabetes medication. Monitoring was conducted on the sample, with documentation of the preparation and consumption of the breadfruit leaves and cinnamon supplement.

In the pretest, HDL levels were examined, followed by a knowledge questionnaire on diabetes mellitus using the Guttman Scale and a medication adherence questionnaire using the MMAS-8. A 24-hour food recall was conducted on the sample for three days to determine their dietary intake. During the intervention, the sample was given a leaflet standardized by the Indonesian Ministry of Health regarding diabetes mellitus, and in the post-test, HDL levels, knowledge, medication adherence, and dietary intake were remeasured.

Study Population

The study population was patients with type 2 diabetes mellitus in the working area of Sudiang Community Health Center and Sudiang Raya Community Health Center. The sample size calculation was 14 people by adding a 30% dropout rate, so the number of samples needed was 21 people for the intervention group and 21 people for the control group. The total sample was 42 people with type 2 diabetes mellitus. The inclusion criteria were samples aged 45-65 years with a duration of diabetes <4 years, no allergy to breadfruit leaves, taking oral medication, willing to consume breadfruit leaf drinks every day for 30 days. The exclusion criteria were pregnancy, being seriously ill, having complicated diseases and not willing to be a sample. The method of recruiting samples was by taking data from the population, namely Type 2 DM patients at the Community Health Center and then selecting patients who fit the inclusion criteria. Respondents who met the inclusion criteria were randomly divided into two groups, with simple random sampling, namely respondents chose papers that had been coded A and B by the researcher, by rolling the papers into a container and shuffling them, then the respondents took one of the papers at random and then gave the paper back to the research student. So that respondents will be divided into 2 groups, namely group A for intervention and group B for control.

Statistical Analysis

Data processing was performed using SPSS 21 computer software to analyse data using univariate, bivariate and multivariate tests. Univariate tests were performed on each variable to obtain an overview of the distribution of respondents. Bivariate tests were performed by comparing the results of HDL level tests before and after the intervention using paired t-tests and Wilcoxon signed-rank tests, as well as independent t-tests and Mann-Whitney tests to examine the treatment between groups. The data obtained was then presented in tables and graphs accompanied by narration.

Univariate analysis was conducted to examine respondent characteristics by calculating the mean and standard deviation. The analysed data were presented in tables or graphs. Bivariate analysis was performed to test hypotheses that would lead to correct and accurate conclusions. The confidence level in this study was 95% and the significance level (α) was 0,5. The first analysis is a data normality test using the *Shapiro-Wilk* test, followed by a *chi-square* test, then a T-test or Wilcoxon test to see the pre-post value changes in each group, and an independent T-test and *Mann Whitney* test to see the comparison of post-test values between groups on HDL levels before and after intervention.

Ethical Approval

This study received approval from the Ethics Committee of Universitas Hasanuddin (No. 1471/ UN4.14.1/TP.01.01/2025). All data collection procedures adhered to the Helsinki Declaration. Each interviewee signed an informed consent form approved by the ethics committee. Respondents signed the informed consent form after the Enumerator had read the Explanation Consent Form (PSP) carefully.

RESULT

The respondents in this study were patients diagnosed with DM for <4 years and taking oral DM medication and aged 35-65 years. The total sample size was 42 people, divided into two groups: 21 in the intervention group and 21 in the control group. They met the exclusion and inclusion criteria, but during the research process, two participants in the intervention group *dropped out* because they experienced changes in coughing and shortness of breath during the intervention period. Therefore, on the advice of the community health centre doctor, they stopped consuming the breadfruit leaf and cinnamon drink until their condition improved.

The results of the study show the characteristics of respondents based on age groups, with the majority of respon-

Table 1. Sample Characteristics

Variable	Intervention		Control		Total	P *Value*
	n (19)	%	n (21)	%		
Age (Years)						
36-45	3	15,8	6	26,8	9	0,543
46-55	9	47,4	7	33,3	16	
56-65	7	36,8	8	38,1	15	
Total	19	100	21	100	40	
Gender						
Female	17	89,5	17	81,0	36	0,451
Male	2	10,5	4	19,0	6	
Total	19	100	21	100	40	
Education						
Primary	3	15,8	4	19,0	7	0,821
Junior High School	5	26,3	4	19,0	9	
High School	9	47,4	12	57,1	21	
Bachelor	2	10,5	1	4,8	3	
Total	19	100	21	100	40	

Table 1 continuation. Sample Characteristics

Variable	Intervention		Control		Total	P *Value*
	n (19)	%	n (21)	%		
Occupation						
Housewife	14	71,7	13	61,9	27	0,585
Civil Servants/Military/Police	2	10,5	4	19,0	6	
Self-employed	1	5,3	3	14,3	4	
Labour	2	10,5	1	4,8	3	
Total	19	100	21	100	40	
Duration of diabetes						
1-2 years	4	21,2	6	28,6	10	0,583
3-4 years	15	78,9	15	71,4	30	
Total	19	100	21	100	40	
BMI						
Underweight	2	10,5	3	14,3	5	0,939
Normal	10	52,6	9	42,9	19	
Overweight	4	21,1	5	23,8	9	
Obesity	3	15,8	4	19,0	7	
Total	19	100	21	100	40	
Adherence to Diabetes Medication						
Low	8	42,1	6	28,6	14	0,412
Moderate	6	31,6	11	52,4	17	
Height	5	26,3	4	19,0	9	
Total	19	100	21	100	40	

dents aged 46-55 years in the intervention group (47,4%) and 56-65 years in the control group (38,1%). The majority were female, with 89,5% in the intervention group and 81% in the control group. The majority of respondents had a high school education, with 47,4% in the intervention group and 57,1% in the control group. The most common occupation was housewife, with 71,7% in the intervention group and 61,9% in the control group. Most respondents had experienced DM for 3-4 years, in the intervention group (78,9%) and the control group (71,4%). Most respondents had a normal BMI, in the intervention group (52,6%) and the control group (42,9%). *The Chi-Square* test results showed that there were no significant differences between the intervention group and the control group for each variable, or that the baseline data was homogeneous, with P values of 0,543, 0,451, 0,585, 0,583, and 0,939, respectively.

The mean HDL variable in the intervention group was 47,95 mg/dL, increasing to 58,68 mg/dL (p value = 0,003), while in the control group, the pre-posttest result was 47,19 mg/dL, increasing to 54,24 mg/dL (p value = 0,013). The change in HDL results (Δ) in the intervention group increased by 10,74 mg/dL, while in the control group it increased by 8,14 mg/dL (p value = 0,506). Although both groups showed a significant increase in HDL levels after the intervention, the between-group difference in Δ HDL was not statistically significant (p=0,506)

In Table 3, the mean knowledge variable of the intervention group pre-posttest was 22,47 to 23,89 with a value (p value = 0,012), while in the control group the results obtained were 20,67 to 22,10 (p value = 0,005).

In Table 3, the mean score for medication adherence in the intervention group increased from 5,74 to 6,68 (p value = 0,010),

Table 2. Differences in HDL Levels Before and After Intervention

HDL	Before (mean + SD)	After (mean + SD)	P Value	Δ
Intervention (n=19)	47,95 ± 15,87	58,68 ± 14,95	**0,00***	10,74 ± 13,32
Control (n=21)	47,19 ± 10,95	52,24 ± 10,19	**0,013***	8,14 ± 11,01
P Value	0,860****	0,036****		0,506***

*Uji T Berpasangan, ***Uji T Independen.

Table 3. Differences in Knowledge, Compliance with DM Medication, dietary intake Before and After Intervention

Variable	Before (mean + SD)	After (mean + SD)	P Value
Knowledge			
Intervention (n=19)	22,47 ± 3,23	23,89 ± 3,619	**0,012***
Control (n=21)	20,67 ± 3,46	22,10 ± 3,223	**0,005***
P Value	0,098***	0,104***	
Compliance			
Intervention (n=19)	5,74 ± 1,996	6.68 ± 1,493	**0,010****
Control (n=21)	6,10 ± 1,814	6.43 ± 1,720	0,144**
P Value	0,581****	0,705****	
Intake			
Energy			
Intervention (n=19)	2485,8 ± 451,10	2393,2 ± 448.52	0,039*
Control (n=21)	2381,9 ± 633,38	2556,8 ± 554.08	0,068**
P Value	0,297****	0,297****	
Protein			
Intervention (n=19)	104,58 ± 18,23	109,32 ± 18,59	0,257*
Control (n=21)	86,52 ± 18,14	100,81 ± 26,55	**0,054****
P Value	0,003***	0,136***	
Fat			
Intervention (n=19)	50,21 ± 37,48	50,32 ± 39,79	0,711**
Control (n=21)	76,81 ± 32,70	78,38 ± 28,42	0,743*
P Value	0,007****	0,003****	

*Uji T Berpasang. **Uji Wilcoxon. ***Uji T Independen. ****Uji Mann Whitneyy.

Table 3 continuation. Differences in Knowledge, Compliance with DM Medication, dietary intake Before and After Intervention

Variable	Before	After	P Value
	(mean + SD)	(mean + SD)	
Carbohydrates			
Intervention (n=19)	414,37 ± 70,52	378,37 ± 77,83	**0,02***
Control (n=21)	317,76 ± 85,54	344,38 ± 111,25	0,198**
P Value	0,000****	0,275****	
Fibre			
Intervention (n=19)	11,37 ± 3,27	10,79 ± 3,80	0,58*
Control (n=21)	8,62 ± 3,50	10,81 ± 9,19	0,060**
P Value	0,003****	0,190****	

*Uji T Berpasang. **Uji Wilcoxon. ***Uji T Independen. ****Uji Mann Whitney.

while in the control group, the mean score increased from 6,10 to 6,43 (p value = 0,144). It can be concluded that there was a significant change in the intervention group with a p-value of 0,010 but no significant change in the control group.

Based on the intake, there were significant differences in intake in the *pre-posttest* intervention group, namely the carbohydrate variable with a value of 0,02 and energy 0,039. Therefore, it can be concluded that there were differences before and after the intervention in the variables of energy and carbohydrate intake (p = <0,5), but there were no significant changes in the other variables.

DISCUSSION

The main variables in this study were fasting blood glucose and *High-Density Lipoprotein* (HDL) in outpatients with diabetes mellitus, with diagnoses categorised according to PERKENI[17]. Body Mass Index (BMI) was measured using anthropometric tools, and a 24-hour recall was conducted three times *pre- and post-test* to measure dietary intake. Knowledge and medication adherence indicators were assessed using a previously validated and structured questionnaire.

In this study, the sample of DM patients consisted mostly of women aged 46-55 years. One of the factors contributing to diabetes mellitus is age, with many type 2 diabetes mellitus patients being over 45 years old due to the decrease in the number of productive β cells with increasing age[18]. Furthermore, as women age, they become more prone to obesity than men.

The average education level in the sample was senior high school (SMA) for 47,4% of the intervention group and 51,1% of the control group. This is in line with research by Adhania[19]. This study found that most respondents were early elderly (46-55 years old), with a high school/equivalent educational background (38,7%), namely 43 people. The majority of the sample's occupation in this study was housewife, both in the intervention and control groups. This is consistent with Adnan's study[20], which found that the majority of the sample were housewives, numbering 22 people (59,5%).

Medication adherence among the intervention group remained low (42,1%), while the control group showed moderate adherence (52,4%). This is in line with the results of a study conducted by Mokolomban[21], which showed that the majority of respondents' medication adherence was in the non-compliant category, namely 28 respondents (62,22%).

In the HDL variable, the intervention group had a pretest score of 47,95 and a posttest score of 58,68 with a p-value of 0,003 (p <0,5), while in the control group, the pretest result was 47,19 and the posttest result was 54,24 with a p-value of 0,013 (p <0,5), indicating a significant increase in both the intervention and control groups. The average increase in HDL in the intervention group was 10,74 mg/dL, while in the control group it was 8,14 mg/dL. However, based on the between-group difference test, a p-value of 0,506 (p > 0,5) was obtained, indicating that there was no significant difference between the increase in HDL levels in the two groups. These results show that although both groups experienced an increase in HDL, the difference in the increase was not large enough to be considered statistically significant.

The flavonoid content in breadfruit leaf extract has an anticholesterol effect on triglyceride, total cholesterol and LDL levels in the blood. The mechanism of action is through increased lipoprotein lipase enzyme activity, which accelerates the hydrolysis of triglycerides and inhibits lipogenic enzymes so that triglycerides are not formed[22]. The results of this study are in line with previous research that examined the effect of breadfruit leaf ethanol extract (*Artocarpus altilis (Parkinson ex F.A. Zorn) Fosberg)* on LDL (*low-density lipoprotein)* levels in male hypercholesterolemic white mice by Tandi[23]. The results of this study indicate that breadfruit leaf ethanol extract has an effect on reducing LDL levels in white mice.

Flavonoids can lower blood glucose levels through their antioxidant properties, which protect *β* cells (insulin producers) from damage and increase insulin sensitivity. Another mechanism by which flavonoids act as antidiabetics is their ability to inhibit GLUT 2 (*Glucose Transporter type* 2), which is the major glucose transporter in the intestine. Inhibition of GLUT 2 leads to a decrease in blood glucose levels. Flavonoids can also inhibit phosphodiesterase, thereby increasing cAMP in pancreatic beta cells. Increased cAMP stimulates the release of protein kinase, which in turn stimulates insulin secretion, leading to increased insulin production and reduced blood glucose levels[24].

The phytochemical test results of dried breadfruit leaf (Artocarpus altilis) methanol extract contain flavonoids, tannins, phenolics and saponins. Flavonoids are a group with low molecular weight based on a 2-phenylchromone nucleus, which is biosynthesised from acetyl/phenylalanine derivatives using the shikimate pathway. Traditionally, flavonoids are classified by their degree of oxidation, C-ring annularity, and ring position linkage. Flavones and flavonols contain the largest number of compounds, representing a small fraction of flavonoids, namely the 2-benzo-γ-pyron category. Quercetin, a flavonol, for example, has been studied the most. Flavanones and flavanonols have saturated C bonds and are often found alongside flavones and flavonols in plants. Isoflavones, such as daidzein, are 3-phenylchromone compounds. As the main precursor in flavonoid biosynthesis, chalcones are the ring-opening isomers of dihydroflavones, responsible for the colouration of plants[25].

Saponins and flavonoids can increase HDL levels and decrease LDL and VLDL (Very Low Density Lipoprotein) levels in rats by inhibiting cholesterol solubility, thereby reducing cholesterol absorption[26]. Based on preclinical studies conducted by Millar[27] using cell cultures and rodent models, it appears that dietary flavonoids affect several HDL functions beyond simple HDL cholesterol content, such as cholesterol efflux and antioxidant capacity.

Significant differences before and after the intervention in this study may also be due to increased knowledge and adherence to DM medication. Based on the knowledge of the intervention group sample, the pretest (mean) was 22,47 and the posttest (mean) was 23,89 with a p-value of 0,012, indicating a change in knowledge before and after the intervention. A similar pattern was observed in the control group, with a mean score of 20,67 on the pretest and 22,10 on the posttest, with a p-value of 0,005, indicating an increase in knowledge before and after the intervention.

Knowledge in managing DM plays an important role because a low level of knowledge can affect a person's lifestyle changes and influence their health. This level of knowledge can shape a person's lifestyle, especially in preventing, recognising, and managing their DM. According to Notoadmodjo[28], a high level of knowledge will improve a person's well-being by enabling them to carry out appropriate care according to their own condition.

Medication adherence is also one of the factors in the incidence of diabetes mellitus. Based on this study, the results of the pretest for the intervention group (mean) were 5,74 and after the posttest 6,68 with a p-value of 0,010, which means that there was a significant change in the intervention group before and after the intervention. Medication adherence is the level of individual participation in following instructions related to prescriptions and restrictions appropriately and done of their own accord. Adherence to the community health centre programme is the patient's action of carrying out all recommendations, orders and restrictions suggested by community health centre staff to help accelerate the patient's recovery process. The level of patient adherence to medication is one of the factors that determines the success of diabetes mellitus therapy.

Changes were also observed in the pretest and posttest samples for the dietary intake variable. Changes occurred in the energy and carbohydrate variables in the intervention group before and after the intervention. The American Diabetes Association 2018 recommends a calorie intake of 1500-1800 kcal for people with diabetes mellitus. Nutritional intake is directly related to controlling blood glucose levels, which come from daily foods containing nutrients such as carbohydrates, proteins, and fats. In the body, the metabolic process of insulin is important in bringing glucose into cells to be used as fuel. The pancreas secretes insulin in individuals with type 2 diabetes mellitus, where insulin secretion may be excessive, insufficient, or normal. However, a reduction in insulin receptors on the cell surface makes it difficult or impossible for glucose to enter the cells, preventing it from being converted into energy[29].

Changes were also observed in the dietary intake variables in the pretest and posttest samples. Based on the dietary intake table for the intervention group, there were changes in the energy and carbohydrate variables before and after the intervention. In the pretest, energy intake (mean) was 2485,8 and after the posttest (mean) was 2392,2 with a p-value of 0,039. This is in line with research Yuliantini[30], which shows that the higher the energy intake, the higher the total cholesterol/HDL levels. The correlation between energy intake and the total cholesterol/HDL ratio obtained a probability value of 0,000 (<0,5), which means that the relationship between energy intake and the total cholesterol/HDL ratio is significant.

The role of blood glucose levels in affecting HDL levels in type 2 diabetes mellitus patients is due to changes in fat metabolism caused by decreased insulin function (insulin resistance). Insulin resistance in type 2 diabetes mellitus patients can cause hormone-sensitive lipase in adipose tissue to become active, thereby increasing triglyceride lipolysis in adipose tissue and producing excess free fatty acids. In the liver, free fatty acids are converted back into triglycerides and become part of VLDL, resulting in triglyceride-rich VLDL. Triglyceride-rich VLDL is exchanged with cholesterol esters from HDL, producing triglyceride-rich HDL but poor in cholesterol esters. This form of HDL cholesterol is more easily catabolised by the kidneys, resulting in a decrease in serum HDL levels.

Limitations in the study were due to the fact that the samples had different schedules, so visits to their homes were arranged to suit their availability. There was a lack of samples participating in the prolanis activity, so monitoring was carried out through direct visits.

CONCLUSION

Breadfruit leaf and cinnamon drink was associated with increased HDL levels, but these changes were not significantly greater than those in the control group. The observed improvements may be partly due to lifestyle education or dietary modifications.

This research can be a reference for other research to determine the effect of breadfruit leaves on diabetes mellitus by examining other variables.

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