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Time-restricted feeding on blood pressure and blood glucose of prolanis participants at primary health care in Tuban, East Java, Indonesia

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Abstract

Introduction: Every year, hypertension claims the lives of over 8 million individuals globally and nearly 1.5 million in Southeast Asia.[6] In addition to hypertension, chronic diseases experienced by people in Indonesia are Diabetes Mellitus. Diabetes and cardiovascular health are closely related, with diabetes patients having a higher chance of acquiring hypertension and vice versa, creating a potentially harmful synergistic interaction. Newer studies have looked into novel dietary approaches to enhance metabolic health and lower the risk of chronic illnesses.

Objective: By shedding light on the intricate relationships between dietary habits, metabolic conditions, and cardiovascular outcomes, this study hopes to advance the development of more specialized and potent treatments for diabetes and hypertension.

Method: A prospective cohort study was conducted on participants of PROLANIS Primary Health Care in Tuban from August – September 2023, using One Way Anova and Kruskal Wallis.

Results: Mean delta BP patients who had a TRF of 12 hours 11.22±9.804, 6 – 12 hours 13.13±10.341 and did not perform TRF 7.40±8.316, p = 0.309. Mean delta blood glucose patients who had a TRF of 12 hours 14.92±10.09, 6 – 12 hours of 7.30±5.708, and who did not perform TRF of 0.20±4.894, p<0.001

Conclusion: TRF significantly lowers blood glucose in patients with diabetes mellitus, but has not had a significant effect on blood pressure in patients with hypertension.

Keywords: Time-Restricted Feeding; Intermittent Fasting; Hypertension; Diabetes Mellitus; Blood Pressure

1. Introduction

High blood pressure, also referred to as hypertension, is a chronic medical disease marked by higher readings that consistently exceed the normal range. It is a significant risk factor for cardiovascular illnesses, such as heart attacks and strokes, and a serious global health concern. As its effects on the cardiovascular system worsen over time, hypertension is known as the "silent killer" because it frequently manifests silently and without obvious signs. The development and aggravation of hypertension are attributed to a combination of lifestyle factors, genetic predisposition, and underlying medical disorders.

According to AHA data from 2011, just 34% of Americans with hypertension—out of 59%—have their condition under control. One out of every four adults is said to have hypertension [1]. It is projected that 1.56 billion persons worldwide

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would have hypertension by 2025 [2]. Every year, hypertension claims the lives of over 8 million individuals globally and nearly 1.5 million in Southeast Asia [3].

With 34.1% of the population suffering from hypertension in 2018, Indonesia emerged as one of Southeast Asia's most affected nations. Gender-wise, Indonesian women account for a greater proportion of hypertension cases (11.57%) than do Indonesian men (6.07%). Age-specific statistics show that the prevalence of hypertension in Indonesia is 69.5% for people over 75, 63.2% for those 65–74 years old, 55.2% for those 55–64 years old, 45.3% for those 45–54 years old, 31.6% for those 35–44 years old, 20.1% for those 25–34 years old, and 13.2% for those 18–24 years old. After North Sulawesi, Yogyakarta, East Kalimantan, and North Kalimantan, DKI Jakarta had the fifth-highest rate of hypertension in 2018 [4].

In addition to hypertension, chronic diseases experienced by people in Indonesia are Diabetes Mellitus. Elevated blood glucose levels are a hallmark of diabetes mellitus, a metabolic condition caused by inadequate insulin synthesis or impaired insulin utilization by the body. Type 1 and Type 2 diabetes are the two main forms that cause major health problems worldwide. Numerous consequences, such as retinopathy, neuropathy, nephropathy, and cardiovascular illnesses are linked to diabetes. Diabetes and cardiovascular health are closely related, with diabetes patients having a higher chance of acquiring hypertension and vice versa, creating a potentially harmful synergistic interaction.

According to WHO estimates, diabetes contributed 6% of Indonesia's 2012 all-cause, all-age mortality [5,6]. According to a 2020 study by the International Diabetes Federation, more than 6% of the 172 million adult population in the nation has diabetes [7]. The nationwide prevalence of diabetes (people 15 years of age and above) has been rising, according to The Indonesian Basic Health Research conducted in 2013 and 2018, with the majority of cases occurring in age groups older than 45. Diabetes types were not distinguished because participants aged 15 and above self-reported their symptoms, blood glucose levels, and self-reported diagnosis [8,9].

Newer studies have looked into novel dietary approaches to enhance metabolic health and lower the risk of chronic illnesses. Time-restricted feeding (TRF) is one method of Time-Restricted Feeding that limits the amount of food consumed each day, usually 8 to 12 hours, and then alternates it with a fasting phase. TRF affects energy expenditure and metabolism in addition to influencing caloric intake and circadian rhythms. Research has demonstrated the potential advantages of TRF as a non-pharmacological treatment for metabolic disorders, with implications for weight control, glucose regulation, and lipid metabolism. A study conducted by Tagde et al in 2022 concluded that Time-Restricted Feeding has been prescribed for the treatment and prevention of cancer and neurological disorders. It has also been proven to successfully reverse diabetes, thyroid, high blood pressure, raised lipid levels, and maintain body mass index [10].

The complex relationship among diabetes, hypertension, and time-restricted feeding emphasizes the necessity of doing thorough study to investigate possible connections and treatment options. Although there is ample evidence linking diabetes and hypertension, research on how novel dietary strategies like time-restricted meals may affect these diseases is still developing. Examining the impact of TRF on blood pressure in diabetics becomes imperative, considering the possibility that lifestyle modifications can supplement medical therapies and enhance general cardiovascular health. By shedding light on the intricate relationships between dietary habits, metabolic conditions, and cardiovascular outcomes, this study hopes to advance the development of more specialized and potent treatments for diabetes and hypertension

2. Material and methods

This study is a prospective cohort study with cross-sectional method. The study was conducted from August to September 2023. The population in this study was hypertensive and diabetes mellitus patients who were chronic disease management program “PROLANIS” participants at the Tuban Primary Health Centre, East Java.

The subjects used were patients with hypertension and diabetes mellitus using non-probability sampling, namely consecutive sampling.

The number of samples was 70 patients who had met the inclusion criteria. The inclusion criteria are patients with hypertension and diabetes mellitus or both who participated in the chronic disease management program "PROLANIS" in August and September 2023, and the exclusion criteria are patients who do not want to be the subject of research and patients who do not attend the "PROLANIS" activities in August and September 2023. The data obtained are secondary data through medical records and data on the results of physical and biochemical examinations of hypertensive and diabetes mellitus patients when they come to the "PROLANIS" activity. The data extracted were gender, BMI, exercise habits, sleep habits, blood pressure and fasting blood sugar, before and after undergoing Time-

Restricted Feeding. Variables of sex, BMI, exercise habits, sleep habits are nominal variables. The variables of blood pressure and blood glucose are numerical variables.

2.1. Data Analyses

Statistical data analysis was performed with SPSS software version 26. Descriptive analysis is carried out to obtain the basic characteristics of the patient. Kolmogorov-Smirnov normality test was performed on the patient's blood pressure and blood sugar data. One Way Anova test and Kruskal Wallis test were performed on blood pressure delta and blood sugar delta data on TRF to find the effectiveness of TRF in controlling blood pressure and blood sugar. Meaning is expressed by a value of $p<0.05$.

3. Results

Of the 70 subjects, 29 male subjects were obtained, and 41 female subjects.

Table 1 Profile of research subjects

Variables	n	%	Mean±SD
Gender			
Male	29	41.4%	-
Female	41	58.6%	-
BMI			
Underweight	4	5.7%	-
Normal	13	18.6%	-
Overweight	26	37.1%	-
Obese gr I	23	32.9%	-
Obese gr II	4	5.7%	-
Exercise			
2 – 3 times/week	13	18.6%	-
1 time/week	32	45.7%	-
Never	25	35.7%	-
Sleep Schedule			
≥8 hours	28	40.0%	-
5 – 7 hours	29	41.4%	-
<5 hours	13	18.6%	-
Time-Restricted Feeding			
12 hours	37	52.9%	-
6 – 12 hours	23	32.9%	-
Does not perform TRF	10	14.3%	-
Systolic Blood Pressure			
Before	-	-	137.51±15.144
After	-	-	126.21±7.989
Delta	-	-	11.30±9.828

Blood Glucose			
Before	-	-	109.11±9.799
After	-	-	98.80±10.067
Delta	-	-	10.31±9.791

A total of 37.1% of patients had BMI Overweight, 32.9% were grade I obese, 18.6% were normal, 5.7% were underweight and the remaining 5.7% were grade II obese. As many as 45.7% exercise 1 time a week, 35.7% never exercise, and only 18.6% exercise 2 to 3 times a week. As many as 40% of patients had adequate sleep time, 41.4% slept in 5 to 7 hours, and 18.6% of patients had a schedule of less than 5 hours a day. As many as 52.9% of patients did Time-Restricted Feeding for 12 hours, 32.9% did it in 6 to 12 hours, and 14.3% of patients did not do Time-Restricted Feeding. Blood pressure measurements before TRF had an average systole value of 137.51 with a standard deviation of 15.144, and an average after TRF of 126.21 with a standard deviation of 7.989, the delta of blood pressure had an average of 11.30 with a standard deviation of 9.828. Blood sugar before TRF had an average of 109.11 with a standard deviation of 9.799, after the average TRF obtained was 98.80 with a standard deviation of 10.067, and the blood glucose delta had an average of 10.31 with a standard deviation of 9.791 (**Table 1.**).

Table 2 Kolmogorov-Smirnov normality test results

Variables	**Statistic**	**df**	**Sig.**
Systolic Blood Pressure			
Before	0.088	70	0.200
After	0.146	70	0.001
Blood Glucose			
Before	0.110	70	0.036
After	0.109	70	0.038
Delta Blood Pressure	0.103	70	0.064
Delta Blood Glucose	0.111	70	0.034

Data normality test was carried out with Kolmogorov-Smirnov and obtained systolic blood pressure data before TRF and delta normally distributed ($p > 0.05$), then One Way Anova test was carried out on these variables. Sytolic blood pressure data after TRF, blood sugar data before TRF, after TRF and delta blood sugar are not normally distributed ($p<0.05$) then continued the Kruskal Wallis test on these variables (Table 2.).

Table 3 Variable correlation test results on delta Blood Pressure and Blood Glucose

Variables	**Δ Blood Pressure**	**P value**	**Δ Blood Glucose**	**P value**
Gender				
Male	11.72±9.331	0.764	11.48±9.672	0.371
Female	11.00±10.269		9.49±9.910	
BMI				
Underweight	7±12.36	<0.001*	7.50±13.72	0.497^
Normal	5.46±7.76		9.15±11.52	
Overweight	7.73±7.63		10.19±9.77	
Obese gr I	19.30±8.61		12.09±8.81	
Obese gr II	11.75±5.06		7.50±8.43	

Exercise				
2 – 3 times/week	6.15±8.194	0.022*	6.77±6.19	0.217^
1 time/week	10.47±8.79		10.44±11.10	
Never	15.04±10.70		12±9.35	
Sleep Schedule				
≥8 hours	10.14±9.34	0.728*	14.46±9.53	0.008^
5 – 7 hours	12.14±10.79		8±7.91	
<5 hours	11.92±9.05		6.54±11.51	

*One Way Annova Test, ^Kruskal Wallis Tests

The data obtained were analysed using the One Way Anova and Kruskal Wallis test methods to determine its significance, obtained significant results on BMI data and exercise on delta systolic blood pressure, and sleep schedule data on delta blood glucose (p<0,05) (**Table 3.**).

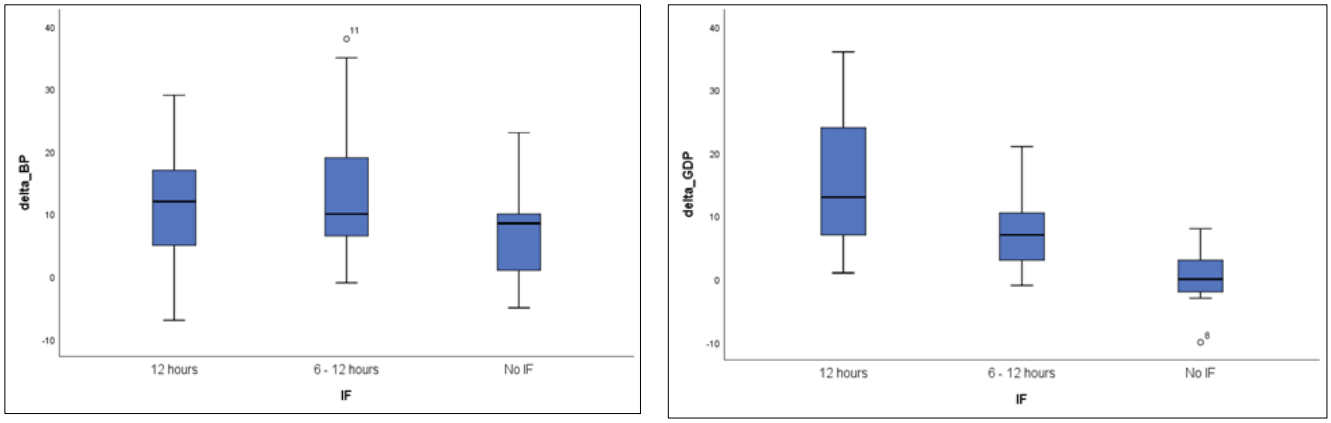

Figure 1 TRF Boxplot against Δ Blood Pressure and Δ Blood Glucose

In figure 1, delta blood pressure was better in the 6-12 hours and 12-hour TRF groups compared to patients who did not undergo TRF at all. Delta blood glucose also appeared to be better in the group of patients who underwent 12-hour and 6-12-hour TRF than patients who did not do TRF at all (Figure 1.).

Table 4 Correlation of TRF to delta Blood Pressure and Blood Glucose

Time-Restricted Feeding	Δ Blood Pressure	P value	Δ Blood Glucose	P value
12 hours	11.22±9.804	0.309	14.92±10.09	<0.001
6 – 12 hours	13.13±10.341		7.30±5.708	
Does not perform TRF	7.40±8.316		0.20±4.894	

Data on Time-Restricted Feeding, delta blood pressure and delta blood glucose obtained were analysed using the One Way Anova and Kruskal Wallis test methods to determine its significance, obtained the highest average delta blood pressure in the group that did TRF 6-12 hours, which was 13.13 with a standard deviation of 10.341. Delta blood glucose was highest in the group that did TRF for 12 hours, which was 14.92 with a standard deviation of 10.09. Significant results were obtained on Time-Restricted Feeding data on delta blood glucose p<0.001, but no significant correlation was found between Time-Restricted Feeding and delta blood pressure p = 0.309 (Table 4.).

4. Discussion

This study examined the relationship between time-restricted feeding of systolic blood pressure and blood sugar levels of patients with hypertension and diabetes mellitus. It was found that the decrease in blood pressure in patients

undergoing TRF was better than patients who did not do TRF at all, but the results of statistical tests found that there was no significant effect between time-restricted feeding or Time-Restricted Feeding on delta systolic blood pressure patients. This is in contrast to the results of a meta-analysis conducted by Wang et al in 2022 which found ten randomized controlled trials, with 694 patients involved. Systolic blood pressure (SBP) was considerably decreased by Time restricted Eating (TRE) (mean difference = −4.15; 95% CI: −6.73, −2.30; P < 0.0001), whereas diastolic blood pressure (DBP) was not significantly affected (mean difference = −2.06; 95% CI: −4.16, 0.02; P = 0.053), and according to this meta-analysis, TRE considerably decreased SBP but had no effect on DBP. An important reason for the observed reduced blood pressure could be the substantial weight loss [11].

Blood pressure displays a diurnal rhythm, which is a typical daily rhythm that is higher in the day than at night. In particular, blood pressure decreases by 10-15% during sleep compared to wakefulness and has a typical morning spike upon awakening [12]. The endogenous circadian rhythm, which is an internally generated, roughly 24-hour cycle that self-sustains in the absence of any environmental stimuli, is not always the same as the observed diurnal rhythm. This is because endogenous circadian rhythmicity is not as important in explaining the observed diurnal rhythm in blood pressure as behavioral and physiological factors are.

One other significant behavioral component that can control blood pressure rhythms is feeding/fasting patterns. Systolic and diastolic blood pressure are lowered during both short-term (48 hours) and long-term (1-41 days) medically supervised fasting [13]. In both normotensive and hypertensive people, fasting has been linked to natriuresis, which can be reversed by glucose delivery. Although the precise mechanisms of fasting-induced natriuresis are still unknown, it has been suggested that the fall in insulin during fasting and the effects of insulin on renal salt retention are the causes. An euglycemic-hyperinsulinemia clamp study supported this theory by showing that insulin administration caused a decrease in urine sodium excretion without affecting glomerular filtration rate, renal blood flow, filtered glucose load, or plasma aldosterone concentration. Numerous mechanisms, including as the stimulation of sodium reabsorption in the kidney, the trophic effect on the migration and proliferation of vascular smooth muscle cells, the upregulation of the angiotensin system, and the tissue-specific modulation of the sympathetic nervous system, have all been proposed as ways in which insulin directly raises blood pressure. The exact cause of hyperinsulinemia and hypertension is still up for debate, though, with insulin treatment lowering blood pressure in obese and diabetic patients but having no effect on blood pressure following correction of hyperinsulinemia following tumor removal in insulinoma patients. On the other hand, changes in glucagon, aldosterone, natriuretic peptides, ketonuria, and sympathetic activity have all been suggested as possible mediators of natriuresis brought on by fasting [14,15].

In this study, some patients also had diabetes mellitus and TRF had a good effect on the patient's blood glucose. There is a significant correlation between TRF and delta blood glucose which can be said that TRF can help control patients' blood sugar as a form of nonmedical therapy. A systematic review conducted by Lin et al in 2022 found similar, seven studies totaling 326 participants were included, comprising two papers with 109 patients with prediabetes and five publications with 217 patients with diabetes. The hours of the TRE windows were 4 to 10 h. The proportion of women varied from 0% to 90%. With no serious adverse effects, TRE may lead to weight loss as well as improvements in insulin sensitivity and plasma glucose. For patients with diabetes and prediabetes, time-restricted eating is a safe and practical intervention that may improve metabolism and the cardiovascular system [16].

A Randomized control trial conducted by Che et al in 2021 found that over the course of 12 weeks, the time-restricted feeding group's hemoglobin A1c and body weight fell (by −1.54% ± 0.19 and −2.98 ± 0.43 kg, respectively) in comparison to the control group ($p < 0.001$). When comparing the time-restricted feeding group to the control group, the homeostatic model assessment of β-cell function and insulin resistance changed (0.73 ± 0.21, $p = 0.005$; − 0.51 ± 0.08, $p = 0.02$, respectively). These findings imply that a 10-hour food restriction increases insulin and blood glucose sensitivity, causes weight loss, lowers the dosage of hypoglycemic medications required, and improves overall quality of life. It can also lower levels of atherosclerotic lipids, which is beneficial for the cardiovascular system [17].

Unfavorable consequences worry a lot of individuals. Reports of identified vomiting (n = 1), headache, diarrhea, and increased thirst (n = 2) were included in a crossover 6-hour TRF trial [18]. A nonsignificant rise in the incidence of side effects, such as nausea, diarrhea, and dizziness, was found in another trial on 8-hour TRF [19]. Furthermore, it was determined that the 10-hour TRF in people with metabolic syndrome had no bearing on the trial because it was linked to muscle soreness (n = 1).

Regarding the mechanism underlying the metabolic improvements caused by TRF, there are multiple theories. According to one study, eating restriction can stop mice from gaining weight, developing dyslipidemia, and developing fatty liver disease by reversing the clock gene phase in their peripheral organs [20]. Other research, however, discovered that the body clock is only marginally impacted by natural eating habits. Alternatively, in mice that are fed regularly, the

brain's central pacemaker might phase the peripheral organs via channels unconnected to feeding behavior. The effects of early (8 am to 5 pm) and late (12 pm to 9 pm) time-restricted feeding on glucose tolerance were examined in a crossover study. Regardless of lunchtime (early or late), the authors showed that time-limited feeding enhanced glycemic responses [21]. Gill S.'s study indicated that energy restriction was the reason for the benefits of TRF, which is in line with our findings. However, no extra effect of daily feeding time was noted [22].

Limitations

This study has several limitations. First, the sample size could be further expanded. Second, the time of intervention was short, and further follow-up is needed to observe the long-term results of TRF. Third, a subgroup design was not implemented for the legacy effect of TRF in our study. Fourth, self-reports, such as food records and adherence to the intervention, were included.

5. Conclusion

There is no relationship between Time-Restricted Feeding to systolic blood pressure patients with hypertension, but there is a relationship between Time-Restricted Feeding to blood glucose patients with diabetes mellitus.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

Author declares there is no conflict of interest during this research.

Statement of ethical approval

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Primary Health Care in Tuban.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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