

The Correlation of Fasting and 2-Hours Postprandial Plasma Glucose with Glycated Hemoglobin as Glycemic Control

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Abstract: Diabetes Mellitus (DM) is one of the non-communicable diseases that are currently increasing in number. One of the indicators that used to describe the longer period of glycemic control in patients with DM is the level of glycated hemoglobin or HbA1c. The purpose of this study was to determine whether in fasting or 2-hours postprandial plasma glucose (PPG) level correlated with HbA1c level. So it can be used as the glycemic control when measurement of the HbA1c is not available. This study is a cross-sectional study, on 60 type 2 diabetes mellitus patients at the University of Sumatera Utara Hospital. Before the examination, respondents are required to fast for 10-12 hours. Examination of fasting plasma glucose (FPG) and 2-hours PPG were performed using a cobas 6000 analyzer with hexokinase and immunoturbidimetry method. HbA1c was measured using high-performance liquid chromatography (HPLC) method. The correlation between FPG with HbA1c and 2-hours PPG with HbA1c was analyzed with the Spearman bivariate correlation test by SPSS 22 version. We found that the mean and SD values of FPG, 2-hours PPG, and HbA1c were 186.31 ± 71.27 , 284.88 ± 92.06 and 8.85 ± 1.73 , respectively. The Spearman bivariate correlation indicated a significant association ($p = 0.005$, $r = 0.357$) between FPG with HbA1c. In this study found that no correlation between 2-hours PPG with HbA1c ($p = 0.780$, $r = 0.036$). We conclusions, FPG indicated as glycemic control better than 2-hours PPG on type 2 diabetic if the HbA1c examination is not available.

1 INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder marked with elevated chronic blood sugar levels (hyperglycemic/ BGLs). This hyperglycemia condition can be affected by insulin resistance syndrome, insulin deficiency, or a combination of both. It leads to impaired metabolism (Rodwell, 2015). DM is a non-communicable disease that every year the incidence of this disease is increases. In year 2015 data by WHO shows that about 415 million people suffer DM and it will be continued to increase in over the last three decades. WHO estimate in year 2040 incidence rate of DM will be 642 million people (WHO, 2016). Oxidative stress is a complications that happen in DM. Oxidative stress will increase lipid peroxide as malondialdehyde (MDA) (Sari, 2018). Increase of lipid peroxide will increase of cell death. Achieving a good glycemic control is an attempt to prevent complications.

Glycemic control in DM patients can be schematically described as the 'glucose triad', with hemoglobin glycate or HbA1c, fasting plasma glucose (FPG), and 2-hours postprandial plasma glucose (PPG) levels (Monnier and Collete, 2009). Among these three components, the HbA1c level examination as a glycemic control is more advantages. The advantage of the HbA1c test is any diet does not influence it, before HbA1c level examination, the patients no need to fasting, (it is so simple for the patients), the results of HbA1c level is stable to monitor hyperglycemic conditions for three months ago and stress conditions not affect the HbA1c levelz (ADA, 2014; Schteingart, 2002). The rate of hemoglobin glycate formation is equivalent to the average amount of blood glucose concentration. When glucose levels rise above normal, the amount of hemoglobin glycate will also increase. The direct association between HbA1c and the average amount of glucose occurs because the erythrocytes

are continuously binding of glucose (Glycosylated) for 120 days of life (Scheingart, 2002).

There is no perfect clinical diagnostic test. HbA1c examination techniques and tools are not available in every hospital or community health center. One of the other limitations is that the cost of HbA1c examination is quite expensive. It is, therefore, necessary to identify whether the HbA1c values are more closely correlated with the fasting plasma glucose or to the 2-hours postprandial plasma glucose levels. This condition is important to know so it can be determined which of the two is preferred as the glycemic control if the HbA1c examination is not possible. Patel 's research (2016) found that HbA1c contributed more to fasting plasma glucose so that FPG and HbA1c were closer to describing glycemic control (Patel ., 2016). The (Ya'cub, 2014) study showed a strong correlation between the 2-hours postprandial plasma glucose and HbA1c values. (Ketema and Kibret, 2015) state that FPG and 2-hours PPG are similarly correlated with HbA1c levels, but the 2-hours postprandial plasma glucose has a closer association with HbA1c than FPG (Ya'cub, 2014; Ketema and Kibret, 2015). Thus, the purpose of the present study was to determine whether HbA1c correlates with fasting plasma glucose or 2-hours postprandial plasma glucose as a glycemic control of type 2 diabetes mellitus (T2DM) in Universitas Sumatera Utara, Hospital, Medan.

2 METHOD

This research used an analytical cross-sectional design. The study were approved by the Ethics Committee of the Faculty of Medicine of the Universitas Sumatera Utara with No. 227/FK USU. The population in this research was type 2 diabetes mellitus patients who were diagnosed by an endocrine specialist based on the criteria established by PERKENI (PERKENI, 2015) in Universitas Sumatera Utara hospital.

The research population consisted of 60 diabetic, and the inclusion criteria were 1) had experienced T2DM for more than six months 2) willing to participate in the research by signing on the presentation sheet after explanation. The exclusion criteria were 1) anemia, hemoglobinopathy 2) had a history of blood transfusion in the last 2-3 months 3) had a disease affecting erythrocyte age and 4) impaired renal function.

Data collection of characteristics such as age, gender and duration of disease were done through interviews using questionnaires. FPG, 2-hours PPG, and HbA1c levels were measured from the blood

plasma of the type 2 DM patients obtained from vena mediana cubiti after fasting for at least 8-12 hours. FPG, 2-hours PPG, and HbA1c were measured at the Integrated Laboratory in the Universitas Sumatera Utara Hospital on the same day. The FPG and 2-hours PPG measurements used the cobas 6000 analyzer with hexokinase and immunoturbidimetry method (Roche Diagnostics, Switzerland). HbA1c was measured using high-performance liquid chromatography (HPLC) method. Then the data was analyzed using the Spearman bivariate correlation test with p-values of < 0.05 were considered significant by SPSS version 22.

3 RESULT AND DISCUSSION

In this study, the characteristics of 60 type 2 DM patients can be seen in Table 1

Table 1: Distribution of respondent characteristics

Variables	N (%)	Mean, SD
Age (years)	-	57.53±9.09
Gender (male/female)	39(65)/21(35)	
Duration of disease (years)	-	7.52±2.80
Fasting blood glucose (mg/dl)	-	186.31±71.27
2-hours postprandial blood glucose (mg/dl)	-	284.88±92.06
HbA1c (%)	-	8.85±1.73

Table 1 shows the mean values of the age of respondents was 57.53 years (SD = 9.09). Age is one of the risk factors for diabetes mellitus. This condition is probably caused by some changes in body composition which is created by the aging process. Aging causes a decline in the pancreatic function that synthesizes insulin (Rochmah, 2009).

In the present research, based on gender found that male respondents group more than female (65% VS 35%). The males are more likely to suffer from DM in this population. The results of this research are not the same as the research conducted by Mihardja which showed that females are two times more likely to have hyperglycemia than males (Mihardja, 2009). Females control the excess energy as fat deposits while male use their excess energy to synthesize proteins. In the female, central obesity and increased body fat will result in a decrease in the action of

insulin in the target tissue, leading to an increase in blood glucose levels (Flier and Maratos-Flier, 2010).

In the present, the mean value of the duration of DM disease is 7.52 years. This value can be seen by reflecting on the mean of FPG, 2-hours PPG and HbA1c levels of the research subjects. On the uncontrolled of DM, the length of the duration of DM will cause the parameters of BGLs will get worse (Sari^b, ., 2018). The mean of the three glycemic parameters were above normal (186.31 mg/dl, 284.88, and 8.85%) with poor HbA1c glycemic control (glycemic controls of either if HbA1c levels <7%, poor, if HbA1c levels >7%) (PERKENI, 2015)

HbA1c is a substance formed from a chemical reaction between glucose and hemoglobin. In HbA1c, the glucose molecules will bind to the N-terminal group on the HbA0 chain of HbA1c, so then the glucose will fuse with the free amino group on valine N-terminal of β hemoglobin (Rodwell, 2015). This binding is called glycosylation. In DM patients, glycosylation of hemoglobin increases proportionately with blood glucose levels during the previous two-three months. In 1976, the HbA1c level was first proposed as an indicator of glucose regulation in diabetic patients. The HbA1c level is mainly determined by two factors which are blood glucose level and erythrocyte age. Since 1980 the measurement of HbA1c levels as a determination of the DM glycemia index has been widely accepted. HbA1c measurement is important for long-term control of glycemic status in diabetic patients to predict a decrease or increase in DM complications (International Expert Committee, 2009)

There is no perfect clinical diagnostic test. HbA1c as a glycemic control does not reflect glycemic changes in a relatively short period, and its accuracy is said to decrease if accompanied by abnormalities of hemoglobin metabolism such as anemia and in patients with thalasemia (Monnier and Collete, 2009). Another problem is it is expensive and not available in most hospitals or health centers.

In addition to the HbA1c test, glycemic control in patients with DM can be done by measuring the FPG and 2-hours PPG levels. These three examinations can schematically be described as 'glucose triads' (Monnier and Collete, 2009). The significance and strength of FPG correlations with HbA1c levels and PPG with HbA1c levels shown in Table 2.

In this study, the Spearman bivariate correlation test showed a significant correlation between FPG and HbA1c levels with weak correlation strength ($p = 0.005$, $r = 0.357$). The FPG level is the BGLs measured after a person undergoes an 8-12 hours fast on the night before the test. The objective of fasting on this test is to reduce the

variability of glucose metabolites resulting from the metabolism of nutrients after meals. Fasting ensures that BGLs are not affected by carbohydrate metabolites from the last intake of nutrients (Rodwell, 2015). Whether there is a correlation between FPG and HbA1c levels so that it can be used to replace HbA1c examination is still debatable. The objective of the FPG examination is as a substitute for the HbA1c examination if the HbA1c test is not available.

Table 2: Correlations between FPG and PPG with HbA1c

Variable	Mean \pm SD mg/dl	p	Correlation (r) with HBA1C
FPG	186.31 \pm 71.2	0.005*	0.357**
2-hours PPG	284.88 \pm 92.0	0.780	0.036**

* $p < 0.01$ level (2-tailed)

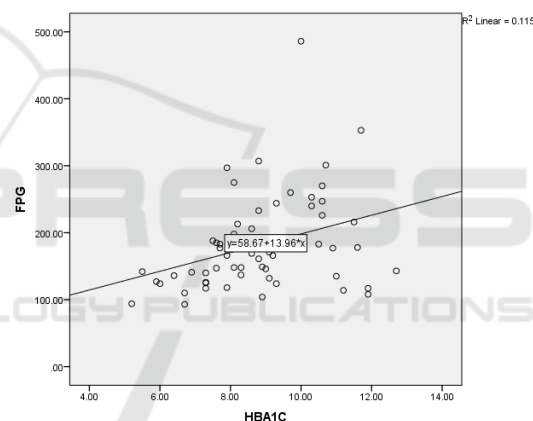


Figure 1. Scatter-plot of FPG with HbA1C levels

The results of the present research are similar to the study by (Akinloye, 2007) who found a significant correlation between FPG and 2-hours PPG levels in patients with type 2 DM with a strong correlation, but no significant in the healthy group (Akinloye, 2017). Similar results were also found in the research by (Suprihartini, 2016) and (Kan, 2015) (Suprihartini, 2016; Khan, 2015). In the study of (Kan, 2015) found a significant correlation between FPG and HbA1c level with regression analysis on both variables showed significance. The significant correlation between the two variables were obtained by cut-off point criteria of HbA1c ≥ 6.5 (Khan, 2015).

Another research of DM patients in Japan shows that FPG is significantly correlated with HbA1c if the cut-off point of HbA1c > 8 (Kikuchi, 2010). The study

by Khatab show there was no significant correlation between FPG and 2-hours PPG in the cut-off point $HbA1c < 8$. FPG appears to be a major contributor to BGLs in uncontrolled diabetes patients ($HbA1c > 8.4\%$) (Khatab, 2010). Research by (Patel, 2016) suggests FPG correlates to HbA1c with levels above $> 7\%$, not below 7% . FPG was also conferred to be the key contributor for glycation of hemoglobin and can assess the shift of glycemic status in diabetics (Patel, 2016).

As well as the debate over the correlation of FPG with HbA1c, the debate over the 2-hours PPG correlation with HbA1c is also much of a basis for research. In the present study, the Spearman correlation between PPG and HbA1c levels show no significant correlation with $p = 0.780$, $r = 0.036$. The results of this study are different from the research conducted by (Sikaris, 2009) which states that there is a significant correlation between PPG with HbA1c and no significant correlation between FPG and HbA1c (Sikaris, 2009). Research by (Ketema and Kibret, 2015) and research by (Shrestha, 2012) found significant correlations between PPG with HbA1c levels and also FPG with HbA1c levels, but PPG found a stronger correlation with HbA1c than FPG (Ketema and Kibret, 2015; Shrestha, 2012). Research by Swetha (2014) also shows a correlation between HbA1c with PPG and FPG, where the r value is $PPG > FPG$. Sensitivity test results show that the specificity obtained by PPG showed better sensitivity (79% vs. 74%) than FPG whereas FPG showed higher specificity (84% vs. 74%) and positive predictive value (87% vs. 80%) compared to PPG (Swetha, 2014).

The 2-hours PPG test is a BGLs examination which is done 2-hours postprandial after fasting for at least 8-12 hours. The 2-hours PPG test was done to see how much of the pancreas or insulin function is made out of the pancreas to regulate the distribution of glucose levels from the blood circulation into the cells. Diabetic patients will experience an increase in BGLs after eating, and because of the insulin, these BGLs will decline within two hours after eating (Rodwell, 2015).

The previous research has found that there is a racial and ethnic variation play a role of HbA1c as a diagnostic test for diabetes. The role of racial and ethnic differences in HbA1c values has been recognized for many years, but so far these differences have generally been associated with differences in care patterns or quality of care (Herman, 2009). Data analysis from the National Health and Nutrition of 1999-2000 showed a difference in mean values of HbA1c levels in the

white race compared to black and Hispanic race. This analysis was done on a population of diabetic and non-diabetic patients. The study reported an average HbA1c value in the white race compared to black, and the Hispanic race was 7.6% VS 8.1% VS 8.2%. This ethnic and racial role in this HbA1c value may affect the correlation between HbA1c and the mean value of either FPG or PPG. The correlation between mean blood glucose and HbA1c may not be the same in all people depending on the ethnicity and race (Herman, 2012)

4 CONCLUSIONS

In this study, HbA1c levels show a significant correlation with FPG levels, not with PPG levels. Hence, as glycemic control, FPG examination may be used instead of HbA1c if the HbA1c test is not available. It should be noted that HbA1c remains the gold standard in the assessment of glycemic control with the availability of the HbA1c method.

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