



## **FASTING BLOOD GLUCOSE LEVELS IN ADULT WOMEN WITH TYPE 2 DIABETES MELLITUS AND ITS ASSOCIATED FACTORS**

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### **ABSTRACT**

Indonesia has the sixth largest number of people with diabetes in the world. This study aimed to investigate association of age of menarche, duration of diabetes, vitamin c (VC) intake and psychological stress with fasting blood glucose (FBG) levels in adult women with type 2 diabetes mellitus (T2DM). Psychological stress was measured using a STAI questionnaire, while anthropometry, duration of diabetes and age of first menarche were assessed using open questionnaires. Vitamin C intake and FBG level were measured using SQ-FFQ and the hexokinase method respectively. Data were analyzed using Spearman Rank correlation and multiple linear regression tests. A total of 188 adult women with T2DM had mean age  $53\pm 5.31$  years old, Body Mass Index (BMI)  $25\pm 3.76$  kg/m<sup>2</sup>, age at menarche  $13.8\pm 1.71$  years old, duration of diabetes  $4.4\pm 3.38$  years and VC  $56.9\pm 46.79$  mg/day. Body Mass Index ( $r=-0.190$   $p=0.011$ ) and VC intake ( $r=-0.153$   $p=0.049$ ) were associated with FBG levels. While, age of menarche, duration of diabetes and psychological stress were not associated with FBG levels.

Keywords : adult women, duration of diabetes, age at menarche , psychological stress, vitamin c intake

### **ABSTRAK**

Indonesia menempati peringkat keenam terbesar jumlah penderita diabetes melitus (DM) di dunia. Tujuan penelitian ini adalah menganalisis hubungan usia menarche, lama menderita DM tipe 2 (DMT2), asupan vitamin c (VC) dan stres psikologis dengan kadar glukosa darah puasa (GDP) pada perempuan dengan DMT2. Stres psikologis diukur menggunakan kuesioner STAI sedangkan data antropometri, lama menderita T2DM dan usia menstruasi dikaji dengan kuisisioner terbuka. Asupan vitamin C ditentukan dengan Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) dan kadar GDP serum diukur dengan metode hexokinase. Data kemudian dianalisis dengan menggunakan Korelasi Spearman dan regresi linier ganda. Sebanyak 188 subjek memiliki rata-rata usia  $53\pm 5,31$  tahun, IMT  $25\pm 3,76$  kg/m<sup>2</sup>, lama menderita DMT2  $4,4\pm 3,38$  tahun, usia mesntruasi  $13,8\pm 1,71$  tahun dan asupan VC  $56,9\pm 46,79$  mg/day. Indeks Massa Tubuh ( $r=-0,190$ ;  $p=0,011$ ) dan asupan VC ( $r=-0,153$ ;  $p=0,049$ ) berhubungan dengan kadar GDP. Sementara itu usia menstruasi, lama menderita DM dan stress psikologi tidak berhubungan dengan kadar GDP.

Kata kunci : asupan vitamin c, lama menderita DM, perempuan dewasa, stres psikologis, usia menarche

## BACKGROUND

The prevalence of diabetes mellitus (DM) has rapidly increased in the last 5 years. In Indonesia, the prevalence of DM is estimated to increase from 10.3 million in 2017 to 16.7 million in 2045 (International Diabetes Federation, 2017). Indonesian Basic Health Research (Riskesmas) showed that the prevalence rate of DM in Central Java, Maluku, South Sulawesi and East Nusa Tenggara reached the national average (2.1%) (Badan Penelitian dan Pengembangan Kesehatan Departemen Kesehatan RI, 2013). According to medical records of General Hospital dr. R. Goeteng Taroenadibrata Purbalingga, Central Java, the number of patients with DM who visited outpatient clinic has increased from 3.047 in 2014 (2.017 women and 1.030 men) to 5.451 in 2016 (3.671 women and 1.780 men).

Health is defined as good physical, mental and social conditions and everyone is able to live productively (Kementerian Kesehatan RI, 2009). From the biological perspective, adolescent girls will normally experience first menstruation at age of 13-14 years. The age of menarche is a sign of puberty so they usually remember it (Must et al., 2002). In a pathological condition, earlier menarche (8-11 years old) increases the risk of polycystic ovary syndrome and type 2 DM (T2DM) (Mueller et al., 2014; Elks et al., 2013). Women with polycystic ovary syndrome have 5-8 times higher risk of developing T2DM than women without polycystic ovary syndrome (Pan, Chen, Tsao, & Chen, 2015). Another study has indicated that higher risk of T2DM in adolescences or young adults was found in women with gestational DM (Mueller et al., 2014).

In general, the majority of T2DM patients does not adhere the prescribed diet. They consume less fruits and vegetables which are recommended for T2DM daily diet (Gudjinu & Sarfo, 2017; Ranasinghe et al., 2015). Adult women with T2DM need 75 mg vitamin C /day (Kementerian Kesehatan RI, 2013), but most patients with T2DM consume vitamin C less than 75 mg/day. As a result, the

daily intake of vitamin C is inadequate. Adequate intake of vitamin C will inhibit leptin secretion from adipocytes and glucose uptake in the small intestine (Garcia-Diaz et al., 2010). A meta-analysis study has documented that high intake fruits and vegetables decreased the incidence of T2DM (Wang, Fang, Gao, Zhang, & Xie, 2016). Thus, inadequate intake of vitamin C will worsen hyperglycemia state in patients with T2DM (Garcia-Diaz et al., 2010).

Diabetic complications like macroangiopathy and microangiopathy are associated with duration of diabetes. Diabetic Peripheral Neuropathy (DPN) is one of the complications often suffered by patients with T2DM. An epidemiological study has revealed that patients suffered T2DM >10 years have 5.82 times higher risk of DPN, compared to patients suffered T2DM <10 years (Maula, 2016). Diabetic retinopathy also has strong correlation with duration of T2DM (Fong et al., 2004).

Besides physical factor, psychological factor also contributes to the T2DM pathogenesis. Around 322 million people in the world experience depression with 5.1% in women and 3.6% in men (World Health Organization, 2017). Sub-syndrome depression and emotional disorders such as dysthymia, anxiety, stress and distress commonly happen in society than primary depression (Chew, 2014). Life pressure, unhealthy lifestyles and rapid technological advances can trigger such stress (Bener, Ozturk, & Yildirim, 2017). Consequently, chronic stress may result in depression. Acute physiological stress response (PSR) does not affect health directly but chronic PSR activates the sympathetic adrenomedullary system (SAM), the hypothalamic pituitary adrenal axis (HPA) and inflammation. In the initial phase of stress response, SAM releases epinephrine and norepinephrine. If stress exists, the HPA will release the glucocorticoid hormone (Kelly & Ismail, 2015). These hormones can cause fat accumulation in the abdominal cavity and increase HbA1C and triglycerides level and decrease High Density Lipoprotein (HDL). In addition, chronic PSR stimulates inflammation through increase of

Interleukin 6 (IL-6) and C-Reactive Protein (CRP) levels, which lead to dysfunction of endothelial cells in the kidneys (Joseph & Golden, 2017). A study showed that moderate to high level of stress increased 2.3 times risk of developing T2DM in the next three years (Harris et al., 2017). Therefore, the objective of this study was to investigate association of age of menarche, vitamin C intake, duration of diabetes, psychological stress with FBG levels in adult women with T2DM.

### METHOD

An analytic observational study with cross sectional approach was conducted in Purbalingga regency. The calculation of sample size used an online formula ([www.openepi.com](http://www.openepi.com)) and it obtained minimum 186 research subjects. Adult women with T2DM who aged 20-60 years old and have lived in Purbalingga more than 5 years were selected as respondents. Respondents were excluded from this study if they had complications, were in pregnancy, used insulin injection and were smoking. This research protocol has been approved by the medical research ethics committee of Faculty of Medicine Universitas Sebelas Maret No. 42 / UN27.6 / KEPK / 2018.

Data of age of menarche and duration of diabetes illness were obtained using open questionnaires while VC intake was measured using Semi Quantitative Food Frequency Questionnaire (SQ-FFQ). The frequency of VC intake was then converted and analyzed using the online nutrient software ([www.nutrisurvey.net](http://www.nutrisurvey.net)). Anthropometric data (body weight and height) were measured using scale (SMIC, China). Psychological stress and FBG level were measured using the State Trait Anxiety Inventory (STAI) questionnaire and the hexokinase method respectively. All collected data were analyzed using Spearman and multiple regression linier tests. The statistical significance was defined with p value less than 0.05.

### RESULT

A total of 216 women with T2DM participated in this study. However, only 188 women had complete data. Table 1

showed the characteristics of the respondents, including age, anthropometric, age of menarche, duration of diabetes, VC intake, psychological stress, blood pressure, oral hypoglycemic (OH) use and FBG levels. Approximately 70% of respondents aged 51-60 years old (mean 53.21±5.31 years old). Based on the BMI category, 23.4% research subjects were overweight and 45.8% were obese. More than half of respondents have suffered T2DM for less than 5 years and consumed less VC. Most respondents experienced moderate level of state and trait anxiety. Prehypertension state was found in around 50% respondents. Less than 10% respondents had normal FBG levels and they commonly used one OH drug.

**Table 1. Characteristics of respondents (n=188)**

Characteristics	n (f)
Age (years) (mean, SD)	53.21±5.31
31 to 40 yo.	4 (2.1%)
41 to 50 yo.	49 (26.1%)
51 to 60 yo.	135 (71.8%)
Weight (kg)	57.94±9.12
Height (m)	1.51±0.05
BMI (kg/m <sup>2</sup> ) (mean, SD)	25.08±3.71
Underweight	1 (0.5%)
Normal	57 (30.3%)
Overweight	44 (23.4%)
Obese I	65 (34.6%)
Obese II	21 (11.2%)
Menarche age (years) (mean, SD)	13.87±1.71
8 to 11	9 (4.8%)
12 to 14	111 (59%)
>14	68 (36.2%)
Duration of diabetes (years) (mean, SD)	4.37±3.38
<5	121 (64.4%)
5 to 9	49 (26.1%)
>10	18 (9.6%)
VC intake (mg/day)	56.9 ±46.79
Less	123 (65.4%)
Enough	17 (9.0%)
Good	7 (3.7%)
More	41 (21.8%)
Psychological stress	
State anxiety	45.88±6.05
Mild	10 (5.3%)
Moderate	173 (92.0%)
Severe	5 (2.7%)
Trait anxiety	44.88±5.04
Mild	20 (10.6%)

Characteristics	n (f)
Moderate	167 (88.8%)
Severe	1 (0.5%)
Systolic	
Normal	18 (9.6%)
Prehypertension	91 (48.4%)
Hypertension st.1	50 (26.6)
Hypertension st.2	29 (15.4%)
Diastolic	
Normal	41 (21.8%)
Prehypertension	88 (46.8%)
Hypertension st.1	42 (22.3%)
Hypertension st.2	17 (9.0%)
FBG (mg/dl)*	181.81±77.24
Hypoglycemic (<70.0)	1 (0.5%)
Normal (70.1-105.0)	15 (8%)
Hyperglycemic (>105.1)	172 (91.5%)
OH use	
Without OH	4 (2.1%)
1 OH	139 (73.9%)
>1 OH	45 (24%)

In this study, Spearman correlation test was used to find out the association of BMI, age of menarche, duration of diabetes illness, VC intake, psychological stress, blood pressure, OH use and age with FBG levels (Table 2). Most variables in this study showed weak and negative associations with FBG levels, except for duration of diabetes and OH use. BMI ( $r=-0.228$ ) and VC intake ( $r=-0.159$ ) were independently associated with FBG levels and it had statistically significance ( $p=0.002$  and  $p=0.03$  respectively). The multiple regression linier test was used to further analyze the associated factors Table 3 showed that BMI and VC intake were together associated with FBG levels although the associations were weak.

**Table 2. Association between predictor variables and FBG level**

Variable	r	p
BMI	-0.228	0.002
Age	-0.015	0.838
Blood pressure		
Systolic	-0.052	0.476
Diastolic	-0.038	0.605
OH use	0.021	0.779
Age of menarche	-0.091	0.251
Duration of diabetes	0.103	0.158
VC intake	-0.159	0.030
Psychological stress		
State anxiety	-0.067	0.359
Trait anxiety	-0.083	0.256

**Table 3. Multiple regression linier test**

Variable	b	95% CI		P
		Lower bound	Upper bound	
BMI	-3.962	-7.013	-0.910	0.011*
VC intake	-0.252	-0.503	-0.002	0.049*
R <sup>2</sup> :3.2%				

## DISCUSSION

The present study revealed that BMI and VC intake were independently associated with FBG levels in women with T2DM. However, age of menarche, duration of diabetes and psychological stress did not associated with FBG levels. Taken together, only BMI and VC intake were associated with FBG levels.

The findings suggest that VC intake influence FBG levels. Study by Jamalana, Rezazadeh, Zeinali and Ghaffari (2015) showed that administration of 1000 mg / day VC for 4 weeks can reduce FBG levels in mice. VC inhibits glucose uptake and lactate production and reduces glycerol releases and leptin secretion in control and insulin-treated cells. In addition, 200 µM VC induces cyclin-dependent kinase inhibitor 1A (Cdkn1a) and caspase 8 (Casp8) expressions, partially inhibits Irs3 and highly reduces Glyceraldehyde-3 phosphate dehydrogenase (Gpdh) expression in insulin-treated cells. Vitamin C also down-regulates extracellular and intracellular reactive oxygen species (Garcia-Diaz et al., 2010). Another study also reported that supplementation of vitamin C, E and Chromium for 6 months could reduce FBG levels, HbA1c, insulin and insulin resistance index (Lai, 2008).

In present study, BMI had a negative relationship with FBG levels. This is in line with a study conducted by Niu et al (2016). Insulin resistance index, C-Reactive Protein levels, Interleukin-6 levels and adipocyte fatty acid-binding protein are higher in obese patients with T2DM than non-obese patients with T2DM (Niu, Li, Wang, Ren, & Bai, 2016). To achieve good control of FBG levels, T2DM patients should follow pharmacological and non-pharmacological regiments. The

pharmacological therapy is the most important strategy if T2DM patients fail to control their FBG levels with non-pharmacological therapies (Perkeni, 2015). All T2DM patients in present study have received OH and they routinely visit primary health services. However, medication adherence was not assessed in this study. According to Polonsky and Henry's study (2016), 80% patients with T2DM do not take OH drugs routinely as prescribed, so their glycemic control is poor. Other limitations of present study are food intake in general and physical activities were not evaluated. Daily diet of patients with T2DM in Indonesia often contain high carbohydrates and lipids such as white rice and fried animal products. Additionally, T2DM patients in Indonesia have low physical activity (Gupta & Jensen, 2012; Gudjinu & Sarfo, 2017).

## CONCLUSION

Vitamin C intake and BMI are associated with FBG levels in adult women with T2DM. The T2DM women should consume vitamin C-rich fruits and vegetables. Further study is required to identify other influencing factors of FBG levels.

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