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Factors Affecting Fasting Blood Glucose in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a metabolic disease which has high morbidity and mortality rates every year. Indonesia has 10.3 million people with diabetes mellitus (DM) in 2017 and becomes the top country for DM worldwide. This study assessed factors affecting fasting blood glucose levels in patients with T2DM.

Methods: Totally, 210 patients with T2DM participated in a cross sectional study. Inclusion criteria were patients suffering from T2DM aged 20-60 years old and lived in Purbalingga and Banjarnegara regencies. Nutritional status was determined using body weight and height, psychological stress by Perceived Stress Scale (PSS-10), smoking habit by a questionnaire and intake of potassium using a 24 hour recall questionnaire. Blood glucose levels were measured by hexokinase method

Results: A correlation between BMI (P=0.02), smoking habits (P=0.04) and potassium intake (P=0.02) with fasting blood glucose levels was noted in T2DM patients; whereas, psychological stress (P=0.85) was not correlated with fasting blood glucose levels.

Conclusion: These findings revealed that body mass index (BMI), smoking habits and potassium intake had positive correlation with fasting blood glucose levels in patients with T2DM.

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Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disease that becomes a global health problem because of its high morbidity and mortality rates every year. The global prevalence of T2DM is estimated to increase from 424 millions in 2017 to 625 millions in 2045 (1). Indonesia has become the sixth rank of countries with diabetes in the world and it reached 10.3 million people in 2017. According to data of Basic Health Research in Indonesia, the prevalence of diabetes in Indonesia was 1.5% in 2013 and increased to 20% in 2018, while the prevalence of diabetes in Central Java Province was 1.6 % (2).

However, the prevalence of T2DM has not been established. Some studies have indicated that modification of internal and external factors plays an important role in reduction of diabetes prevalence (3, 4). Franz et al. (2015) reported that individuals with obesity have twice higher risk to suffer from T2DM than individuals with normal weight. Fat accumulation in such obese individuals resulted in light or moderate chronic inflammation, by which it can reduce insulin sensitivity. Therefore, it will

increase blood glucose level in blood circulation (5-7).

Psychological stress and smoking habits are other risk factors of diabetes, which have extensively been studied in recent years (8-10). In physiological conditions, stress responses are regulated by two different pathways including sympathetic nervous system for quick responses and neuroendocrine system for prolonged system. Briefly, stress stimulus will activate hypothalamic nuclei through the correlus nucleus and stimulate the medula adrenal gland to release catecolamin hormones such as adrenalin, noradrenalin and dopamine. If the stress is persistent, the hypothalamus-pituitary adrenal axis (HPA) will be activated and the hypothalamus produces corticotropin-releasing hormone to stimulate the anterior pituitary and the cortex adrenal, releasing the cortisol hormone (8, 10, 11).

It was shown that light or moderate stress will induce the release of growth hormones and endorphins. Furthermore, prolonged and severe stress led to a higher release of cortisol hormone, which can increase blood glucose level through gluconeogenesis and inhibition of insulin action (10, 12). Some evidences indicated that smoking can increase inflammation and oxidative stress, resulting in interferences in pancreatic β cells function (8). High nicotine levels in cigarettes may lead to insulin resistance by inhibition of insulin secretion (14).

Those nicotine compounds interact with the nicotinic acetylcolinesterase (NAchR) receptor and result in Mechanistic target of rapamycin (mTOR) activation (13). As a result, excessive mTOR expression will up-regulate the insulin receptor substrate-1 (IRS-1) Ser 636 insulin receptor so that insulin does not recognize its receptors (14). In normal condition, potasium is required for electrolyte water balance and is located in intracellular compartments. In human body, potassium levels equal to 53.8 mmol/kg are tightly maintained in a narrow range of 3.5–5.0 mmol/L, a balance between potassium intake and excretion through the kidney and the intestinal tract (15).

Serum insulin levels are also needed to transport potassium into cells, but the affinity is lower than the affinity of glucose uptake (16). Progressively, higher blood glucose level is proportionally associated with higher potassium levels too. Insulin deficiency in diabetic patients causes translocation of intra-cellular potassium to the extra-cellular compartments due to hypertonicity (17). Therefore, the objective of this study was to investigate the association of factors affecting fasting blood glucose levels in patients with T2DM.

Materials and Methods

The research protocol was approved by Ethical Committee of Medical Research, Faculty of Medicine, Universitas Sebelas Maret numberred 43/UN27.6/KEPK/2018 (sim-epk.keppkn.kemkes.go.id). All selected participants filled and signed the informed consent to follow this study. Research participants in this cross sectional study were enrolled using an Open Epi Programe (http://www.openepi.com) with 95% confidence interval and 80% power and were selected using a purposive sampling method.

A total of 210 patients with T2DM aged 20-60 years old and were members of diabetes organizations (Persadia and Prolanis) in Purbalingga and Banjarnegara Regencies met the inclusion criteria. Selected research partipants were excluded from this study if having diabetes complications and comobidities (such as asthma, tuberculosis and HIV/AIDS) and used insulin injections. Antropometric data consisted of body weight (kg) and height (m), which were measured using a weight scale (GEA, Indonesia) and microtoice scale (GEA, Indonesia).

The Perceived Stress Scale (PSS-10) questionnaire was used to measure psychological stress, while open questionnaire was used to collect data of smoking habits. Potasium intake was obtained from the 24-hour food recall and converted into mg daily intake with a modified nutrisurvey software (www.nutrisurvey.de). Adequate potassium intake was based on recommended dietary allowance (RDA) in Indonesia for participants who aged 20-60 years old with T2DM (4,700 mg/day).

Research participants had adequate potassium intake, if consumed 90-119% from RDA, 70-79% moderate deficiency, <70% severe deficiency and >120% excessive intake. All participants underwent 8 hour fasting in the night before taken their blood venous in the following morning. Around 3 mL blood sample was taken from lower arm vein of the participants, which was used to measure fasting blood glucose level with the hexokinase method at the clinical pathology laboratorium, of Dr. Goteng Taraoenadibrata Hospital, Purbalingga.

Their fasting blood glucose levels were categorized into 3 groups of 70.0-105.0 mg/dL as normal, <70.0 mg/dL as hypoglycemia and >105 mg/dL as hyperglycemia. All collected data were statistically analyzed using a SPSS software (Statistical Package for Social Sciences, version 16, Chicago, IL, USA, www.spssindonesia.com). All numeric data were presented as mean±SD, whereas categorical data (age, smoking habit, duration of ilnes and Taking oral anti-diabetic drugs) were presented as frequency and percentages.

To analyze the relationship of BMI, psychological stress, duration of illness, age and potasium intake

with fasting blood glucose levels, the Pearson correlation test was used with the significan value of p less than 0.05. For further investigation, some confounding factors such as age, duration of diabetes illnes and oral diabetes drugs were analyzed using the regression linier test instead of BMI, psychological stress, smoking habit and potasium intake.

Results

The basic characteristics of participants with T2DM were similar except for smoking habits and fasting blood glucose levels (Table 1). The average age of T2DM participants was 52.67±5.2 years with 49% males and 51% females and the majority of participants had a range of age betwen 46 and 55 years old. Antropometric data showed that 47.6% of participants were overweight and 14.7% had obesity. Most participants had moderate stress and the majority of male participants were active smokers.

Around seventy percent of participants had <5 years duration of ilnes and had high fasting blood glucose levels. In Table 2, the relationship between BMI, psychological stress, smoking habits and potassium intake with fasting blood glucose levels were presented. The increased BMI (r=0.141, P=0.04), smoking habits (r=0.113, P=0.03) and potassium intake (r=0.156, P=0.02) had a significant relationship with fasting blood glucose level, whereas psychological stress did not show any correlation with fasting blood glucose levels in T2DM patients. In Table 3 based on multivariate analysis and linear regression test results, BMI variables, smoking habits and potassium intake showed a positive relationship with increased fasting blood glucose levels in T2DM patients.

Table 1: Basic characteristics of patients with type 2 diabetes mellitus

Variable	Male (n: 103) %	Female (n: 107) %	Total (n: 210) %	Mean±SD
Age (Years)				
36-45	11 (5.8)	10 (4.2)	21 (10.0)	52.7±5.2
46-55	54 (25.7)	65 (31.0)	119 (56.7)	
55-60	38 (18.1)	32 (15.2)	70 (33.3)	
Duration of illness (years)				
<5	75 (35.7)	72 (34.0)	147 (70.0)	4.3±3.0
5-10	23 (11.0)	33 (15.7)	56 (26.7)	
>10	5 (2.3)	2 (1.0)	7 (3.3)	
Taking oral anti-diabetic Drugs				
1	52 (24.7)	55 (26.3	107 (51.0)	
>1	49 (23.3)	54 (25.7)	103 (49.0	
Body mass index (kg/(m)^2)				
Underweight	5 (2.3)	2 (1.0)	7 (3.3)	24.1±3.4
Normal	38 (18.1)	34 (16.2)	72 (34.3)	
Overweight	45 (21.4)	55 (26.2)	100 (47.6)	
Obese 1	13 (6.1)	15 (7.2)	28 (13.3)	
Obese 2	2 (1.0)	1 (0.4)	3 (1.4)	
Psychological Stress				
(PSS 10)	12 (5.025)	12 (5.025)	22 (10.5)	19.6±4.2
Mild	90 (42.025)	98 (46.025)	188 (89.5)	
Moderate				
Smoking habits				
Yes	70 (33.3)	0 (0)	70 (33.3)	
No	33 (15.7)	107 (51.0)	140 (66.7)	
Potasium intake (mg/d)				
Severe deficiency	11 (5.4)	28 (13.3)	39 (18.6)	945.8±3.3
Moderate deficiency	14 (6.7)	15 (7.1)	29 (13.8)	
Mild deficiency	21 (10.0)	28 (13.3)	49 (23.3)	
Normal	8 (3.8)	16 (7.6)	24 (11.4)	
Over intake	49 (23.3)	20 (9.6)	69 (32.9)	
Fasting blood glucose (mg/dL)				
Hypoglycemia	4 (1.5)	1 (0.4)	5 (1.9)	173.7±54.8
Normal	8 (3.9)	5 (9.0)	27 (12.9)	
Hyperglycemia	91 (43.2)	101 (48.0)	179 (85.2)	

Table 2: Correlation of BMI, psychological stress, smoking habits and potasium intake, with fasting blood glucose levels in T2DM

Variable	r*	P**
BMI	0.141	0.041
Psychological stress	0.006	0.929
Smoking habits	0.113	0.032
Potasium intake	0.156	0.023

*Correlation coefficient, **P value Pearson, BMI: Body mass index, T2DM: Type 2 diabetes mellitus

Table 3: Regression linear between BMI, psychological stress, smoking habits, potasium intake and confounding variable with fasting blood glucose levels

Variable	r*	95%CI	P**
Age	0.078	0.014-2.812	0.252
BMI	1.590	4.748- 432	0.019
Psychological stress	0.174	1.959-1.611	0.848
Smoking habits	1.870	25.610- 5.870	0.042
Potassium intake	0.025	0.047-0.003	0.024
Duration of DM illness	0.078	1.011-3.834	0.252
Taking oral anti-diabetic drugs	1.321	5.835-23.917	0.232

*Regression coefficient, **P value regression linear, BMI: Body mass index, DM: Diabetes mellitus, CI: Confidence interval

Discussion

In this study, we found that BMI, smoking habits and potassium intake were significantly correlated with fasting blood glucose levels in T2DM patients, whereas psychological stress was not associated. These Findings were in line with previous studies. Onyesom et al. (2013) reported a positive but weak correlation between BMI and blood glucose levels among the male subjects (r=0.43); while female subjects showed a positive and strong correlation (r=0.53) (18).

In addition, a person who has obesity, he may have a higher risk of unstable blood glucose level compared to a person who has normal body weight (6, 7, 9). Theoretically, smoking habit is a risk factor of T2DM. The results of our study indicated that smoking habit was also a risk factor of T2DM and in line with previous studies (8, 18-20). Smoking can cause damage of beta pancreatic cells (8, 19), leading to disruption of insulin production (8, 20). Furthermore, nicotine in cigarettes inhibits insulin secretion by interacting with NAchR receptor and stimulating mTOR action (13, 21-24).

Increased mTOR activities induce IRS-1 Ser 636 expression and result in insulin resistance in skeletal and fat cells in patients with T2DM (14, 21-24). In the physiological condition, potassium is required for cellular depolarization including pancreatic beta cells (25-27). From our study, a significant relationship was observed between potassium intake and fasting blood glucose level in patients with T2DM. This finding is in accordance with a prospective cohort study conducted by Colditz and colleagues (1992). They investigated women (n=84,360; 34-59 years) from the Nurse's Health Study for six-years and found that high potassium intake may be associated with a decreased risk for developing T2DM in women with BMI less than 29, but in women with BMI equal or more than 29 were inverse (28).

Psychological stress and fasting blood glucose level did not illustrate any significant relationship in patients with T2DM. The findings in this study revealed that patients who experienced psychological stress were more likely to be in the moderate category. The results of this study are in line with previous research which stated that chronic psychological stress can affect the activation of the hypothalamic-pituitary-adrenal (HPA) axis by increasing the hormone cortisol, activation of the autonomic nervous system and inflammation that causes insulin resistance (10, 29, 30). Psychological stress is due to a pressure factor and unpreparedness in the person's soul to accept the situation (31, 32).

Conclusion

The findings in this study had implications that BMI, smoking habits and potassium intake, have a positive correlation with fasting blood glucose levels in patients with T2DM.

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Conflict of Interest

None declared.

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