Von Willebrand Factor Levels and Control Glycemic Type 2 Diabetes Mellitus Patients

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Abstract: Diabetes Mellituswas disorder metabolic syndrome, characterized by hyperglycemia, which was caused by insulin secretion defect.The chronic hyperglicemia dan insulin resistence caused increasing blood vessel permeability and endothelial cell damage. Von willebrand factor (vWF) was synthesized by endothelial cell.The aim of the study was knowingassociation between von Willebrand factor (VWF) levels and control glycemic base on Fasting Blood Sugar and Haemoglicosylate (Hba1c) at Type 2 diabetes mellituspatients. The sutudy was cross-sectional design , was conducted on 40 type 2 Diabetes Mellitus patients who attended Primary Health Care Clinic in Binjai city, Sumatera Utara, Indonesia.The inclusion criteteria of the samples was patients with age > 40 years old, (both sexes). Body Mass Index, Blood Pressure,disease history and socioeconomic status were recorded. The laboratory parameters including Hba1c, Fasting Blood Sugar Levels. Examining Fasting Blood Sugar Levels by using portable measuring instrument, and Hba1c was examined by Thamrin clinical laboratory. We found there was correlation significant between FBS with Hba1c and correlation significant FBS and VWF.

1 INTRODUCTION

Diabetes Melitus (DM) was caused by the body's inability to produce the insulin as needed or because of ineffective use of insulinor the both. This is characterized by increasing blod sugar level or hyperglycemia and the development of chronic vascular complications (Perkeni,2011,IDF 5th).There was an increasing the prevalence the diabetes mellitus with type 2 the worldwide and it was association with obesity. The number of diabetics in Indonesia is 7 th in the world. The prevalence of diabetes in Indonesia has been diagnosed 1,4%, this will continue increasing (Rikesdas,2013).The evidence of diabetes mellitus with a potent cardiovascular risk factor have annual mean mortality rate of 5.4% (Rikesdas,2013). Men with diabetes have two-fold to three-fold increase in Coronary Artery Disease (CAD) compared with non-diabetics (Donnelly R,et al, 2000). It affects between 1% and 10% of most population, although in some areas of the world up to 50% of the population has diabetes (Vaccaro O et al,1998). WHO estimated 21.527.000 Indonesia population will suffer from diabetes mellitus in 2030 (WHO).As we know for many years that the complication of diabetes mellitus associated with cardiovascular, cerebrovascular and peripheral vascular disease. Because of chronic hyperglycemic and insulin resitance caused increasing permeability of blood vessel and disorder endothelial cell. Type 2 diabetes patients have early development of abnormal endothelial function, it caused vasocontriction, inflammation cell accumulated,migration of smooth muscle cell and increased cytokine production,which results in plaque development. And then it was caused platelet hyperactivity, aggressive atherosclerosis,a propensity for adverse arterial remodeling, enhanced cellular and matrix proliferation after arterial injury and impaired fibrinolysis with tendency for thrombosis and inflammation. The earliest manifestation of endothelial dysfunction was profound arteriopathy the result of the diabetic state (K.G.M.M. Alberti, 2013).

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Type 2 diabetes mellitus patients have a higher incidence of thrombotic complications (Beckman JA, 2002). Many factors that have been proposed explaining the observed prothrombotic state. In connection with prothrombotic state, endothelial activation has been shown to occur in patients suffering from type 2 diabetes (Frankel DS, 2008). Von Willebrand factor (vWF) is a large glycoprotein produced by vascular endothelial cells that mediates platelet adhesion to injured endothelium, the first step in thrombus formation. yWF also serves as the carrier protein for coagulation factor VIII (Natali A, 2006).Given essential role in thrombosis and is frequently used as marker for endothelial activation and damage (Sadler JE, 1991,Ruggeri ZM, 1999)

Recently many researches that was found that Von Willebrand Factor has been associated with insulin resistance and type 2 diabetes mellitus (Blann AD, 2006, Meigs JB et al, 2006).The previous study in type 2 diabetes mellitus patients it was found the increased circulating levels of plasma vWF, it have been attributed to enhanced endothelial cell release from a potentially greater intracellular storage pool and to increased endothelial synthesis (Ostergard T et al, 2006, Porta M, 1982). The aim of this study was to knowing association von Willebrand factor levels and glycemic control at type 2 diabetes mellitus

2 MATERIAL AND METHODS

In the study,a total of 72 patients with type 2 diabetes mellitus were recruited from Primary Health Care in Binjai city, North Sumatera, Indonesia. The number of the samples was calculated using the formula $n=N/1 +N (d^2)$. This was conducted from April to July 2018. In accordance with the inclusion criteria which are,aged > 40 years old and cooperative and have a will to join this research and exclusion criteria which are, using diuretic and the middle of cancer therapy. This research was approved by Health Research Ethical Committee, Medical Faculty of University Sumatera Utara/H.Adam Malik General Hospital by number 591/TGL/KEPK FK USU-RSUP HAM /2018. Patients were informed with the detail of the study and written consent was obtained from the patients before they participated in the study.We measured height and weight with the subjects standing in light clothes . Body mass index was calculated as the weight in kilograms divided by square of the height in meters (kg/m^2).We examine the blood pressure values as mean of two measurements after the subjects had been seated for at least five minutes. The patients fasted overnight to provide a blood specimen. Blood samples were collected (using syringe) and transferred to Thamrin clinical laboratory immediately to be conducted glycosylated haemoglobin test by Alere Afinion as 100 Analyzer . We examined glycosylated haemoglobin test for patients because of this examination as gold standard for diabetes mellitus patients. Fasting blood sugar of samples we examined by using portable measuring instrument (Gluco DR).We measured the Von Willebrand Factor levels with an ELISA assay in laboratory in Medical Faculty, Universitas Sumatera Utara.

The Examination Von Willebrand Factor levels in the serum which allow samples to clot for 2 hours at room temperature or overnight at 4° C before centrifugation for 15 min at 1000x g g at 2-8° C. We collect the supernatant to carry out the assay. We used the blood collection tubes should be disposable and be non-endotoxin. Average the duplicate readings for each standard and samples, then subtract the average zero standard optical density. Plot a four parameter logistic curve on log-log graph paper, with standard concentration on the x-axis and Optical Density (OD) values on the y-axis. If the samples have been diluted, the concentration calculated from the standard curve must be multiplied by dilution factor. If the OD of the samples surpasses the upper limit of the standard curve, we must do re-test it with an appropriate dilution. The actual concentration is calculated concentration multiplied by dilution factor. The Optical Density (OD) was determined using a microplate reader set to 450nm.

3 STASTICAL ANALYSIS

All data were presented by using SPSS software, version 24.The continuous data was expressed as mean ±standard deviation (SD). The correlation were done by Pearson correlation analysis, using correlation test, p-value < 0.05 was considered to be statistically significant.

4 RESULT

Among 72 known type 2 Diabetes Mellitus patients 30 people were male (41.7%) and 42 people were female (58.3%). The characteristic of the subjects of

this study are shown in the table 1. Subjects in this study were not bellow 40 years old. Maximum age of the samples were 79 years old and minimum age were 40 years old. Maximum of Body Mass Index of the samples were 32.86 kg/m^2 and minimum were 16.02 kg/m^2 . Maximum of waist size of the samples were 107 cm and minimum were 73 cm. Maximum of the Fasting Blood Sugar (FBS) of the patients were 600 mg/dL and Minimum were 85 mg/dL. Maximum of the Hba1c of patients were 14% and minimum were 6% and Maximum of the Von Willebrand Factor Level of the patients were 35.10 ng/mL and minimum were 2.16 ng/mL. The range of fasting plasma levels of vWF at baseline was from 0.64 to 5.35 U/ml.

The Pearson's correlation coefficient for the correlation between von Willebrand Factor levels and and Hba1c showed a negative correlation but a positive correlation between von Willebrand Factor levels and fasting blood sugar levels and showed a positive correlation between Fasting Blood Sugar Levels and Hba1c ($p<0.005$.)

Table 1: Baseline characteristic of 72 patients type 2 diabetes mellitus

	Minimum	Maximum	Mean	SD
Age (y.o)	40	79	58.31	8.82
BMI (kg/m^2)	16.02	32.86	24.33	2
Waist size (cm)	73	107	91.32	3.34
FBS (mg/dL)	85	600	243.0	8.18
Hba1C (%)	6	14	1	102.
VWF (mg/dL)	2.16	35.10	9.501	2
			11.14	1.90
				4
				6.84

Table 2 : Pearson Correlation vWF and glycemic control (Hba1c,FBS)

		Hba1c	
vWF	FBS		
Hba1c	Pearson Correlation 1		0.002
389**			
Sig.(2-tailed)			0.985
0.001			
N		72	72
72			
vWF	Pearson Correlation	0.002	1
0.250*			
	Sig.(2-tailed)		985**
034			
	N	72	72
72			
FBS	Pearson Correlation		389**
250*	1		
	Sig.(2-tailed)	001	034
	N	72	72
72			

**.Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

5 DISCUSSION

The aim of study was to knowing association between von Willebrand factor levels and glycemic control at type 2 diabetes mellitus. As we know that von Willebrand factor was one of the marker for endothelial dysfunction (Porta M, 2006).The primary physiologic function of von Willebrand factor is to maintain haemostatic balance in the vasculature, but because the endothelium is a primary source of von Willebrand factor elevated levels reflect stimulation or injury to endothelial cells (Goldberg RB et al, 2012).This research showed that there was significant correlation between vWF level with fasting blood sugar as glycemic control, as we know that vWF were significantly higher in patients with type 2 diabetes mellitus. Another study by Umadevi B et al showed that a significant increase in plasma levels of von Willebrand factor (vWF) in patients with type 2 DM compared to normal, which suggests that there is significant endothelial injury in type 2 diabetes mellitus patients (Tian J et al, 2012).And the present study shows that type 2 diabetes mellitus patients have significant endothelial injury as assessed by increased levels of plasma von Willebrand Factor (vWF) and these are probably at risk of developing cardiovascular complications in the future.

6 CONCLUSION

There was significant correlation between vWF level with fasting blood sugar at type 2 diabetes mellitus patients.

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REFFERENCES

Beckman JA, Creager MA, Libby P, Diabetes and atherosclerosis epidemiology, pathophysiology, and management. JAMA 2002;287 (19):2570- 81.

Blann AD,Plasma von Willebrand factor, thrombosis, and the endothelium: the first 30 years. Thromb Haemost,2006;95:49-55.

Donnelly R, Emslie-Smith AM, Gardner ID, et al. Vascular complication of diabetes. BMJ 2000;320:1062-6.

Frankel DS, Meigs JB, Massaro JM, Wilson PW, O'Donnell CJ, D'Agostino RB, Tofler GH, Von Willebrand Factor, type 2 diabetes mellitus, and risk of cardiovascular disease: the Framingham offspring study. Circuation.2008;118:2533-2539.doi: 10.1161/CIRCULATIONAHA.108.792986.[PMC free article] [Pubmed] [Cross Ref].

Goldberg RB. Cytokine and cytokine-like inflammation markers, endothelial dysfunction and imbalanced coagulation in development of diabetes and its complications. J.Cin Endocrinol Metab 2009;(9):3171-82.

International diabetes Federation (IDF) atlas 5th edition. Available from: http://www.idf.org/diabetesatlas/5e/the-global-burden

K.G.M.M. Alberti and P.Zimmet, "Epidemiology: global burden of disease-where does diabetes mellitus fit in?" *Nature Reviews Endocrinology*, vol.9, no.5,pp.258-260,2013.View at Publisher . View at Google Scholar . View at Scopus

Meigs JB, O'Donnell CJ, Tofler GH, Benjamin EJ, Fox CS, Lipinska I, Nathan DM , Sullivan LM, D'AGostino RB, Wilson PW. Haemostatic markers of endothelial dysfunction and risk of incident type 2 diabetes , the Framingham Offspring Study.*Metabolism* , 2006;55:1133-1140.

Natali A, Toschi E, Baldeweg S,et al. Clustering of insulin resistance with vascular dysfunction and low-grade inflammation in type 2 diabetes . Diabetes, 2006;55:1133-1140.

Ostergard T, Nyhol B, Hansen TK,Rasmussen LM, Ingerslev J,Sorensen KE, Botker HE, Saltin B, Schmitz O. Endothelial function and biochemical vascular markers in first- degree relatives of type diabetic patients: the effect of exercise training . *Metabolism*, 2006;55:530-537.

PERKENI 2011. Konsensus pengelolaan dan pencegahan diabetes melitus tipe 2.di indonesia, PB. PERKENI

Porta M. Availability of endothelial von Willebrand factor and platelet function in diabetic patients infused with a vasopressin analogue. *Diabetologia*.1982;23:452-455.

Prevention of diabetes mellitus.Report of WHO study group. World Health Organ Tech Rep Ser 1994;844:1-100.

Riskesdas 2013. Riset kesehatan dasar Riskesdas 2013.

Ruggeri ZM. Structure and function of von Willebrand factor. Thromb Haemost 1999;82:576-84. [PubMed:10605754].

Sadler JE, Von Willebrand factor. J Biol Chem. 1991;266:22777-22780

Tian J, Wangf J, Li Y, et al. Endothelial function in patients with newly diagnosed type 2 diabetes receiving eary intensive insulin therapy . American Journal of Hipertension 2012;25 (12):1242-8.

Umadevi B, Roopakala M.S, Wilma Delphine Silvia C.R, Prasanna Kumar K.M. Role of Von Willebrand Factor In Type 2 Diabetes Mellitus Patients. J.Evolution Med.Dent.Sci 2016;5: 81.DOI:10.14260/jemds/20161372

Vaccaro O, Stamler J, Neaton JD. Sixteen- year coronary mortality in black and white men with diabetes screened for the multiple risk factor intervention trial (MRFIT). Int.J.Epidemiol 1998;27 (4):636-41.