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Stages of BMI, Glucose Control, and Endothelial Cell Activation in Malignancy with Diabetes Patients

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Abstract

BACKGROUND: Abnormalities of glucose metabolism in diabetes can be an independent risk factor for the development and prognosis of cancer; it caused endothelial cell activation, inflammatory reactions. Hemostatic disorders, thrombosis, and various human organ damaged that will increase the morbidity and mortality rate. Diabetes was predicted to reach 552 million by 2030 in conjunction with rapid social and cultural changes. With the changes in lifestyle, body mass index (BMI) plays an important role in increasing the risk of metabolic diseases like diabetes type 2. One sign of endothelial cell activation is an increase in Von Willebrand Factor, which can be an early sign of increased coagulation activation until thrombosis occurs.

AIM: The aim of the study was to determine the correlation between BMI, glucose control, and endothelial cell activation in malignancy with diabetes patients.

METHODS: This is a case-control study with eighty samples. BMI, HbA1C, vWF, and D'dimer were measured.

RESULTS: There is a statistical significant correlation between blood glucose and HbA1C ($p = 0.00$), blood glucose and BMI ($p = 0.037$), HbA1C an BMI ($p = 0.029$), HbA1C and vWF ($p = 0.03$), HbA1C and age ($p = 0.009$), D'Dimer and vWF ($p = 0.00$), and age and BMI ($p = -0.019$), but no statistical significant between vWF and BMI ($p = 0.97$), vWF and age ($p = 0.36$).

CONCLUSIONS: There was an increased risk of thrombosis in malignancy with diabetes cases. BMI showed a significant correlation with blood glucose controlled, blood glucose control showed a significant correlation with the activation of the endothelial cell and hypercoagulable state.

Introduction

Diabetes mellitus (DM) and malignancy are two chronic diseases which have a major impact on health population, both contribute to the increase of morbidity and mortality worldwide. DM is a chronic metabolic disease presented with chronic hyperglycemia due to insufficiency or resistance of insulin. The prolonged hyperglycemia will impair and damaged various human organ systems [1], [2]. Abnormalities of glucose metabolism in diabetes can be an independent risk factor for the development and prognosis of cancer [3], [4]. Hyperinsulinemia, insulin resistance, obesity, medications, and diet may play an important role. Several studies have shown the increased incidence of several cancers such as pancreas, colon, kidney, breast, stomach, liver, and endometrium in diabetes [5] and it has been reported that chronic hyperglycemia can promote tumor cell proliferation and metastasis in type 2 diabetes [6].

The prevalence of diabetes is globally increasing and is considered as an endemic chronic disease [7]. Diabetes, in conjunction with rapid social and cultural changes, aging population, urbanization, lifestyle [8], has affected more than 366 million, and it was predicted to reach 552 million by 2030 [7]. Increased in body mass index (BMI) is associated with an increased risk of metabolic diseases like diabetes type 2 [9].

Chronic hyperglycemia in diabetes can cause endothelial cell activation, inflammatory reactions. Hemostatic disorders, thrombosis, and various human organ damaged that will increase the morbidity and mortality rate [10]. One of the markers of endothelial cell activation is Von Willebrand Factor, a multimeric glycoprotein synthesized by megakaryocytes and endothelial cells [11]. Increased levels of vWF levels indicate hypercoagulable state [12] and are associated with the progression of micro and macrovascular dysfunction [13], [14]. Cancer was known as a prothrombotic disease [15], and most of the cause of death in cancer was thrombosis [16]. Abnormal vascularization of the tumor will result in endothelial cell activation. Changes in tumor biology, activation of coagulation, and inflammation all explain the pathogenesis of thrombosis in cancer patients [17], [18].

Aim

This study was to evaluate the relation between stages of BMI, glucose control, and endothelial cell activation in malignancy with diabetic patients.

Methods

This is a case-control group with eighty samples, collected from Murni Teguh Memorial Hospital Medan Indonesia. All malignancy cases are solid tumor and were diagnosed with pathology reports. Diabetes was determined by the random blood glucose level above 140 mg/dl and HbA1C above or equal to 6.5.

Laboratory measurements

Blood glucose was measured using spectrophotometry, HbA1C using HPLC assay, HbA1C was used to determine the blood glucose controlled level. vWF was measured to determine the endothelial cell activation using enzyme-linked immunosorbent assay (ELISA). D'dimer was used to determine the hypercoagulable state, this was measured using the ELISA method. The measurement was done after fasting at least 9 h. BMI was determined by calculating body weight and height according to the standardized protocols [19]. Data were analyzed using SPSS 22.

Ethics, consent, and permissions

This study has been approved by the Medical Ethical Committee of Medical Faculty Universitas Sumatera Utara Medan Indonesia. All participants were provided with written informed consent before the study.

Results

Eighty samples of malignancy with diabetes were recruited. They were 38.8% male and 61.3% female with the ages rank from 30 to 73 years old. The mean age is 54 years old. The mean HbA1C was 6.3, there were 77.5% samples with well-controlled blood glucose level and 22.5% samples with a bad controlled glucose level. The mean BMI was 24, the distribution of BMI with normal weight was 71.3%, overweight 21.3%, and obese 7.5%. The mean vWF was 53, with 30% of samples develop endothelial cell activation, and the mean D'dimer was 1.1, with 67.5% samples were in hypercoagulable state (Table 1).

Spearman's rho correlation was used to determine the correlation between variables, there is a statistical significant between blood glucose and HbA1C ($p = 0.00$), blood glucose and BMI ($p = 0.037$), HbA1C and BMI ($p = 0.029$), HbA1C and vWF ($p = 0.03$), HbA1C and age ($p = 0.009$), D'dimer and vWF ($p = 0.00$), and age and BMI ($p = -0.019$), but no statistical significant between vWF and BMI ($p = 0.97$), vWF and age ($p = 0.36$).

Discussion

In this study, most of the blood glucose levels were well controlled. BMI has a significant correlation with age and blood glucose control, this also has been proved by Satwanti *et al*. [20], they stated that BMI was found to be associated with age independently. Blood glucose has a positive correlation with BMI has been reported by Neelam *et al*. [21]. There was activation of the endothelial cell at thirty percent of the samples (normal limit above 50 IU), and this has been reported by Mark *et al* (2003) and Horowitz and Brenner (2008). vWF also reported to increase at several conditions such as inflammation and infection disorders. Blood glucose control has a significant correlation with endothelial cell activation, age, and BMI, as has been reported before by other researches, with the activation of the endothelial cell will lead to hypercoagulable state; in this study, we got 67.5% cases with activation of coagulation.

Table 1: Laboratory and descriptive tests of the samples

Variable	n	Minimum	Maximum	Mean	SD
HbA1C (%)	80	2.40	12.70	6.3	2.07
D'dimer (mcg/ml)	80	0.13	4.50	1.1	0.96
Blood glucose (mg/dl)	80	50	635	183	109.5
BMI	80	17.70	38.71	24	4.09
Body weight (kg)	80	40	85	55	9.6
vWF (iu)	80	1.00	436.60	53	71.7
Age (years)	80	30	73	54	9.4

Conclusions

With all the above findings, there was an increased risk of thrombosis in malignancy with diabetes cases that can worsen the prognosis of the disease. BMI showed a significant correlation with blood glucose controlled, blood glucose control showed a significant correlation with the activation of the endothelial cell and hypercoagulable state.

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