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Hypercoagulable State and Glycemic Control in Diabetic Patients with Malignancy

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Abstract

BACKGROUND: Diabetes and malignancy are two chronic diseases that have a major impact on the healthy population in developing countries, both contribute to the increase of morbidity and mortality of the patients. Diabetes presented with hyperglycemia due to insufficiency or resistance of insulin has been associated with an increased risk of thrombosis. Malignancy or cancer is number two killer in the developing countries after infectious diseases, one of the most common cause of death in cancer despite the disease itself is thrombosis, which occurred frequently as cancer cause changes in tumor biology, abnormal vascularisation, endothelial dysfunction, activation of coagulation and inflammation. Poor glucose control reflects by HbA1C has a significant correlation with a hypercoagulable state.

AIM: This study was to evaluate the relation between hypercoagulable state and glycemic control in diabetic patients with malignancy.

METHODS: This is a case control study, eighty samples diabetes (40 samples were diabetes with malignancy) were collected from private hospitals and clinics. HbA1c, blood glucose level and Ddimer were measured.

RESULTS: The forty five percent of the blood glucose level of the samples was not well controlled. Sixty five percent of the samples in this group were norm weight, overweight 20% and obese 10%. The Ddimer levels were elevated in both groups and there was a significant correlation between HbA1C and Ddimer (p-0.046), blood glucose and age (p = 0.017).

CONCLUSION: Chronic hyperglycemia will increase the risk of hypercoagulable state, that will also increase the morbidity and mortality rate in diabetes with malignancy patients.

Introduction

Diabetes Mellitus (DM) and malignancy are two chronic diseases that have major impact on health population, both contribute to the increase of morbidity and mortality of the patients. Diabetes Mellitus, a chronic metabolic disorder presented with hyperglycemia due to insufficiency or resistency of insulin, is considered one of the largest non-infectious health problems in the world, it is estimated there will be 300 million of people with diabetes in 2025 with the most in developing countries [1].

The prolonged hyperglycemia in diabetes will impaired and damaged various human organ systems [2], [3]. The endothelial cell dysfunction, haemostatic disorders, hypercoagulable state and thrombosis were the main complications that increase the morbidity in diabetes [4].

Malignancy or cancer is number two killer in developing countries after infectious diseases. One of the most common cause of death in cancer despite the disease itself is thrombosis [5] which occurred occurred frequently as cancer cause changes in tumor biology, abnormal vascularisation, endothelial dysfunction, activation of coagulation and inflammation, besides the cancer itself causes increase activity of the procoagulant factors such as tissue factors, platelets and leucocytes. These explain the pathogenesis of thrombosis in cancer patients [6], [7]. Tumor tissue can activate blood coagulation and malignancy transformation are also involved in the

regulation of caogulant factors in tumor cells [8].

Patients with malignancy and DM shared the same variety of co-morbid which can increase morbidity and death, one of the most common is thrombosis that involving both the arteries and veins. Abnormalities in endothelial cells and a tendency of thrombosis may cause atherosclerosis and its complications. In normal circumstances endothelial cells produce the substances needed to maintain blood vessel homeostasis and preventing thrombosis [9].

Overweight and obesity that affect the majority of adults are increasing rapidly worldwide, driving the global diabetes epidemic [9]. Increase in body fat is generally associated with increased risk of metabolic diseases likes diabetes type 2 [10]. Body mass index were used to determine the presence or absence of obesity related comorbid disease [11].

This study was aimed to evaluate the relation between hypercoagulable state and glycemic control in diabetic patients with malignancy.

Methods

This is a case control study, eighty samples diabetes (40 samples were diabetes with malignancy) were collected from private hospitals and clinics. Malignancy cases were all solid tumor, diagnosed with pathology report, and diabetes was determined with the blood glucose ad random above 140 mg/dl and HbA1C.

Laboratory measurements

HbA1C was measured using an HPLC assay, blood glucose using spectrophotometry, hypercoagulable state was estimated by determining the Ddimer level using ELISA (Enzyme Linked immunosorbent assay).

Body mass index were determined by calculating body weight and height according to the standardized protocols [24]. All datas were analyzed by using SPSS 22.

Ethics, consent, and permissions

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

Results

Eighty samples with diabetes, in which 40 samples were with malignancy, were recruited.

Table 1: Characteristic of the diabetes with malignancy samples

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Hba1c	40	8.70	5.4	14.1	8.5	2.6
Blood glucose	40	465	92	557	242	122
Ddimer	40	4.28	.2	4.5	1.3	1.04
BMI	40	23.37	14	38	25	4.08
Age	40	40	45	85	60	8.9

In this group they were 40 % male and 60 % female with the ages range from 45 years to 85 years old. Forty five percent of the blood sugar of the patients were poorly controlled. Sixty-two-point five percent of the patients have normal BMI, 27.5% overweight and 2.5% underweight, less are obese patients.

Table 2: Characteristic of the diabetes samples

	N	Range	Minimum	Maximum	Mean	Std. Deviation
HbA1C	40	10.3	2.4	12.7	7.6	2.3
Blood glucose	40	552	83	635	260	105.53
Ddimer	40	4.4	.13	4.5	1.3	1.1
BMI	40	19	19	39	25	5
Age	40	36	37	73	57	8.8

In the diabetic group there were 40 % male and 60% female. Forty five percent of the samples blood glucose was not well controlled as in the diabetes with malignancy group. Sixty five percent of the samples in this group were normoweight, overweight 20% and obese 10%, no underweight was found in this group.

The Ddimer levels were elevated in groups, 60% in the diabetes with malignancy group and 75% in the diabetes group. Mann-Whitney U test was used to analyze the HbA1c and Ddimer level between the diabetes patients and diabetes with malignancy patients, and it did not showed statistical significant ($p = 0.08$, $p = 0.44$). Correlation was calculated using the Spearman's Rho correlation, and there was significant correlation between HbA1C and Ddimer (p-0.046), blood glucose and age ($p = 0.017$).

In both group most of the samples were normoweight (60-62.5%), only in the diabetes with malignancy group got the underweight samples (2.5%).

Discussion

In this study, around forty five percent of the samples' blood glucose were poorly controlled, this may because of the bad compliance, the disease itself like malignancy and medications. The chronic

uncontrollable glucose levels will worsen the hypercogulable state, this can be seen from the Ddimer levels that elevated in both groups, and from the statistical significant of the correlation between HbA1C and Ddimer.

Body mass index did not showed any correlation with another variable in this study, maybe most of the samples were normoweight.

In conclusion, most of the blood glucose levels were not well controlled in both groups. This should be encouraged in the health care system to improve the control of blood glucose. Both groups showed hypercoagulable state which can be seen from elevated of the Ddimer though did not showed statistical significant between group.

There was statistical correlation between HbA1C and Ddimer, this should be an issue to be aware as chronic hyperglycemia will increased the risk of hypercoagulable, also the morbidity and mortality rate in diabetes with malignancy patients.

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