Metabolic Syndrome and Atherosclerotic Risk Factors as Determinants of Blood Sugar Control in Diabetic Patients: A Retrospective Cohort Study

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Objective: *To examine the effects of metabolic syndrome and atherosclerotic risk factors on blood sugar control in diabetic patients.*
Material and Method: *This present retrospective cohort study of two hundreds of medical records of diabetes patients treated at the outpatient internal medicine department during the year 2006-2007. Data were collected using a case record form containing biochemical profile characteristics of patients and metabolic components by the World Health Organization (WHO) criteria. The affecting factors to optimal treatment were analyzed to give descriptive (percent = %, mean, SD, median, range) and inferential statistics (odds ratio = OR).*
Results: *There were 200 diabetic patients included in the present study with males of 30.5% and females of 69.5%. Patients who have a higher number of components of criteria of metabolic syndrome tend to have difficulties in controlling their blood sugar (OR for 4 vs. < 3 components: 4.78 95% CI = 1.14-19.97). Patients with younger age groups are more likely to fail to control their blood sugar with OR of 3.87 (95% CI = 1.53-9.76).*
Conclusion: *Diabetic patients who have higher components of metabolic syndrome and younger age tend to have difficulties in controlling their blood sugar. However, the association between having atherosclerotic risk factors and outcome of blood sugar control is inconclusive and needs further studies with a larger sample size.*

Keywords: *Metabolic syndrome, Diabetes mellitus type 2, Type 2 DM, Atherosclerotic, Risk factor*

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Prevalence of diabetes mellitus has been increasing worldwide because of the aging population and globalization. WHO projected the number of individuals with diabetes will be elevated from 135 million in 1995 to 300 million in 2025[1]. This global trend has also occurred in Thailand and the disease has become a public health problem. A survey of multi-national study reported the prevalence of type 2 diabetes of 9.8%, which was twice the number that was forecasted by the WHO[2].

In addition to hyperglycemia itself, diabetic patients also bring other components of the so called metabolic syndrome, *i.e.*, hypertension, dyslipidemia, abdominal obesity and the consequent cardiovascular diseases[3]. Metabolic syndrome could be attributed to hyperglycemia and increased risk of micro- and macrovascular diseases[4], with similar proportional effects on disease risk observed in Western[5] and Asian[6] populations. As such, diabetes is likely to be an important determinant of the vascular disease

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burden in countries such as Thailand, where coronary heart disease has been the leading cause of death for over a decade [7]

One of the goals of treatment of diabetes mellitus is to control blood sugar at optimal levels and metabolic-atherogenic risk factors (lipid level, blood pressure and insulin resistance) to reduction of micro- and macrovascular complication and cardiovascular disease[8-13]. Many factors have shown to be associated with control of blood sugar in these patients including insulin resistance in obesity, a number of factors of metabolic syndrome, ages, educator team and endocrinologist in the diabetic clinic[14-17]. Although information on patients' biochemical profiles and characteristics could be useful for predicting degree of achievement of the treatment. It is important to investigate the factors affecting treatment of diabetes with metabolic syndrome.

Objective

To examine the effects of metabolic syndrome and atherosclerotic risk factors on blood sugar control in diabetic patients.

Material and Method

The present study was designed as a retrospective cohort study. Two hundreds diabetes patients were selected from the outpatient internal medicine department at HRH Princess Mahachakri Sirindhorn Medical Center, Faculty of Medicine of Srinakharinwirot University in 2006-2007. The study protocol was approved by the medicine faculty. Srinakharinwirot University, Ethics committee. Data from medical records of individual patients were extracted using case record forms containing information of age, sex, weight, height, attending diabetes clinic, hypertension status, smoking status, physical inactivity, family history of heart disease, dyslipidemia status, fasting blood sugar, hemoglobin A_{1c} (HbA_{1c}), cholesterol, triglyceride(TG), LDL and HDL. Data from medical records of the same group of patients were extracted again after one-year interval (2007-2008) for fasting blood sugar, HbA_{1c}, cholesterol, triglyceride, LDL and HDL. Metabolic syndrome in the present study was defined according to WHO criteria in these following components such as impaired glucose metabolic or diabetes mellitus, obesity (BMI $\geq$ 30 or waist/hip ratio>0.9 in male or > 0.85 in female), triglyceride $\geq$ 150 mg/dl or HDL-C < 40 mg/dl, blood pressure $\geq$ 140/90 mmHg. Atherosclerotic risk factors included smoking, physical inactivity and family history of cardiovascular death. HbA_{1c} was indicated as the outcome of blood sugar control and the level of HbA_{1c} of 7% or more were classified as uncontrolled diabetes. The sample size was estimated to be able to reject the null hypothesis that this relative risk equals 1 with the power of 0.8. The Type 1 error probability associated with this test of this null hypothesis is 0.05. Number of patients without exposure of interest was estimated to be three fold of the exposure group and outcome of interest was expected to be 15% in the non-exposure group with the predicted relative risk of 2.0. The data were analyzed by SPSS version 11.5. Percent mean with SD and median with range were calculated for descriptive statistics and logistic regressions were used to estimate relative risk between factors and outcomes of treatment. A p-value of < 0.05 was considered statistically significant.

Results

There were 200 diabetic patients in total included in the present study with 30.5% of males and 69.5% of females. Table 1 describes demographic and clinical characteristics of patients. Nine percent were current smokers. Physical inactivity was reported

Table 1. Characteristics of diabetes patients with metabolic syndrome

Characteristics	Categories	Number	%
Sex	Male	61	30.5
	Female	139	69.5
Hypertension status	No	1	0.5
	Yes	199	99.5
Smoking status	Never smoking	155	78.0
	Ever smoking	27	14.0
	Current smoker	18	9.0
Physical inactivity	Yes	165	83.0
	No	35	18.0
Family history of heart disease	Yes	125	63.0
	No	75	38.0
Body mass index (kg/m^2)	18.5-24.99	34	17.0
	25-29.99	71	35.5
	30-34.99	60	30.0
	35 or more	35	17.5
	Median (range)	29.8	18.7-50.1
	Mean (SD)	30.14	5.4
Age	Mean (SD)	62.83	11.47
Weight	Mean (SD)	76.08	14.3
Height	Mean (SD)	1.59	0.07

among 83% of the patients. Seventeen percent of patients were classified as normal weight. All of the patients had fasting blood sugar, cholesterol, triglyceride and LDL higher than normal level. Table 2 shows biochemical profiles of patients at baseline and after one-year interval. Fasting blood sugar of 31% of the subjects was reduced to the normal level while 42% had a reduction of HbA_{1c} to below 7%. Reductions of blood lipid levels were found in a large number of patients for triglyceride (68.5%), cholesterol (53.5%) and LDL (48.5%) but only 14% of improvement was found for HDL levels. In Table 3, factors associated with uncontrolled blood sugar measured by high HbA_{1c} were analyzed, it was found that patients who had 4 components of metabolic syndrome (hypertension, body mass index, TG and HDL) had a significantly

Table 2. Outcome of treatment of diabetic patients with metabolic syndrome

Biochemical outcome	Categories	At time start		After following-up	
		Number	(%)	Number	(%)
Fasting blood sugar	<110 mg/dl	0	0	63	31.5
	110+ mg/dl	200	100	137	68.5
	Total	200	100	200	100
HbA1c	<7 (%)	1	0.5	85	42.5
	7+ (%)	199	99.5	115	57.5
	Total	200	100	200	100
Cholesterol	<199 mg/dl	0	0	137	68.5
	200+ mg/dl	200	100	63	31.5
	Total	200	100	200	100
Triglyceride	<150 mg/dl	0	0	107	53.5
	150+ mg/dl	200	100	93	46.5
	Total	200	100	200	100
LDL	<100 mg/dl	0	0	97	48.5
	100+ mg/dl	200	100	103	51.5
	Total	200	100	200	100
HDL	>40 mg/dl	95	47.5	123	61.5
	≤40 mg/dl	105	52.5	77	38.5
	Total	200	100	200	100

Table 3. Factors associated with high levels of HbA1c in diabetic patients with metabolic syndrome

Variables	Categories	HbA1c < 7%, No. (%)	HbA1c 7%+, No. (%)	Adjusted OR[1]	95% CI
Metabolic syndrome[2]	Two components or less	33 (38.8)	45 (39.1)	1.0	
	Three components	44 (51.8)	55 (47.8)	1.40	0.58-3.36
	Four components	8 (9.4)	15 (13.0)	4.78	1.14-19.97
Atherosclerotic risk factor[3]	No risk	15 (17.6)	9 (7.8)	1.0	
	One risk or more	70 (82.4)	106 (92.2)	2.33	0.69-7.92
Age	60 years or more	57 (67.1)	72 (62.6)		
	Less than 60 year	28 (32.9)	43 (37.4)	3.87	1.53-9.76
Attending diabetes clinic	Attendance	75 (88.2)	25 (21.7)		
	No attendance	10 (11.8)	90 (78.3)	47.54	17.91-126.20

[1] Odds ratios (ORs) were adjusted for sex and attending diabetes clinic; [2] Metabolic syndrome includes hypertension, body mass index, triglyceride (TG) and HDL; [3] Atherosclerotic risk factors composes of smoking, physical inactivity and family history of cardiovascular death

increased risk of 4.78 times compared to those who had any two components or less. For having at least one atherosclerotic risk factors comprising of smoking, physical inactivity and family history of cardiovascular death, the risk was 2.33 time compared to having no risks; however this was not statistically significant. Patients who were aged less than 60 years were found to have an elevated risk of poor diabetic control more than older ones with statistically significant OR of 3.84 (95% CI = 1.53-9.76). In addition, not attending diabetic patient clinics was found to be associated with higher risk of failure to control blood sugar by 47.5 times compared to patients who attended the clinic.

Discussion

The present study was aimed to investigate the effects of metabolic syndrome and atherosclerotic risk factors on outcome of treatment of diabetes. The results showed that patients who have higher components of metabolic syndrome tend to have difficulties in controlling their blood sugar. Probably these components had caused insulin resistance, therefore resulting in high blood sugar[18]. In a healthy population, the metabolic syndrome is a strong predictor for development of type 2 diabetes with five times increased risk[19]. The underlying cause of the metabolic syndrome continues to challenge the experts but both insulin resistance and central obesity are considered significant factors[20,21]. Genetics, physical inactivity, aging, a pro-inflammatory state and hormonal changes may also have a causal effect, but the role of these may depend on ethnic group[22,23].

In relation to components of metabolic syndrome, obesity, now thought to affect 50 to 60% of a nation's population[24], it suggested there is an association with insulin resistance. Obesity contributes to hypertension, high serum cholesterol, low HDL-C and hyperglycemia, and is independently associated with higher CVD risk[21,25,26]. The mechanism by which excessive body fat causes insulin resistance and impairs glucose metabolism is not clearly defined but fat stores (particularly visceral adipose tissue) are an important cause of increased free fatty acid (FFA) and TG in the skeletal muscle, which impairs insulin secretion, raising blood glucose levels and the likelihood of developing diabetes. Excess adipose tissue (particularly the visceral fat tissue in the abdomen) also releases inflammatory cytokines that increase insulin resistance in the body's skeletal muscles. Furthermore, control obesity is also associated with a decreased production of adiponectin, which is the adipose-specific, collagen-like molecule found to have anti-diabetic, anti-atherosclerotic and anti-inflammatory functions[27].

The present findings also indicate that diabetes patients who have at least one component of atherosclerotic risk factors are more likely to be uncontrolled of HbA_{1c} in these patients with relative risk of 2.33 (0.69-7.92); however, the result was not statistically significant. This is possibly due to limited number of subjects in the present study. This large effect size of the association suggests further studies with adequate power of study.

In addition, the present findings showed that the patients in younger age groups are more likely to fail to control blood sugar the fact that our younger patients related more to obesity which causes insulin resistance and affects the control of blood sugar in these groups[23]. Although, the present study has limitations in analyzing the behavior and life-style between the two patient groups such as physical inactivity, atherogenic diet, emotion and stress the conclusion of these results needs to substantiate assumptions in the future.

Finally, the present results showed that attending a diabetic clinic has a considerably high benefit in controlling diabetes possibly because the clinic provided aggressive and holistic management in these patients. It is suggested that adjustment to change behavior and life-style such as diet, exercise and weight reduction and use of proper medicine could result in improved insulin sensitivity[23]. These components might explain the advantage of attending the diabetic clinic[25].

The present study, however, has some limitations. Firstly, the sample size was rather small due to the number of patients in the clinic; nevertheless, this problem could be solved by a designed collaborative multi-center study with other hospitals. Secondly, some of the patients were prevalent cases of diabetes patients who had already been treated; therefore, some of the past treatment may affect the results. Thirdly, some of the behavioral factors of the patients such as dietary control were not included due to retrospective design.

Conclusion

Diabetic patients who have higher components of metabolic syndrome and younger age tend to have difficulties in controlling their blood sugar. The evidence of the association between having atherosclerotic risk factors and outcome of blood sugar

control was inconclusive and further studies with a larger sample size are suggested. This preliminary information could be used for screening diabetic patients who probably need aggressive monitoring and holistic management by an educator team.

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ภาวะ metabolic syndrome และปัจจัยเสี่ยงของการเกิดหลอดเลือดแข็ง กับการเป็นปัจจัยบ่งชี้การควบคุมระดับน้ำตาลในผู้ป่วยเบาหวานในการศึกษาแบบติดตามผู้ป่วยย้อนหลัง

สมลักษณ์ จึงสมาน, สุธีร์ รัตนะมงคลกุล

วัตถุประสงค์*: เพื่อผลภาวะ metabolic syndrome และปัจจัยเสี่ยงของการเกิดหลอดเลือดแข็งต่อการควบคุมระดับน้ำตาลในผู้ป่วยเบาหวาน*

วัสดุและวิธีการ*: การศึกษานี้เป็นเก็บข้อมูลผู้ป่วยเบาหวาน จากเวชระเบียนประวัติผู้ป่วยนอก ที่มารับการรักษาที่ห้องตรวจผู้ป่วยนอกแผนกอายุรศาสตร์ระหว่างปี พ.ศ. 2549 ถึง พ.ศ. 2550 ข้อมูลถูกเก็บโดยใช้แบบฟอร์มการเก็บข้อมูลที่ประกอบด้วยข้อมูลพื้นฐานของผู้ป่วย, ข้อมูลพื้นฐานทางห้องปฏิบัติการของผู้ป่วยด้านระดับน้ำตาลและองค์ประกอบทาง metabolic syndrome โดยใช้เกณฑ์ของ WHO ปัจจัยที่อาจส่งผลต่อการควบคุมระดับน้ำตาลถูกวิเคราะห์เป็นค่าทางสถิติ*

ผลการศึกษา*: ประกอบด้วยผู้ป่วยเบาหวานจำนวน 200 คน เป็นชาย ร้อยละ 30.5 และหญิง ร้อยละ 69.5 ผลของการศึกษาสรุปได้ว่าปัจจัย 3 ประการ ที่อาจมีผลต่อการควบคุมระดับน้ำตาลในผู้ป่วยเบาหวานที่มีภาวะ metabolic syndrome คือ จำนวนองค์ประกอบของภาวะ metabolic syndrome ที่มาก (OR: 4.78; 95%CI: 1.14-19.97), ผู้ป่วยกลุ่มอายุน้อย (OR: 3.87; 95% CI: 1.53-9.76) และการไม่ได้รับการรักษาโดยคลินิกเบาหวาน (OR: 47.54; 95% CI: 17.91-126.20)*

สรุป*: ผู้ป่วยเบาหวานที่มีจำนวนองค์ประกอบของภาวะ metabolic syndrome มาก, อายุน้อย และอ้วน มีแนวโน้มควบคุมระดับน้ำตาลยาก สำหรับความสัมพันธ์ระหว่างปัจจัยเสี่ยงของการเกิดหลอดเลือดแข็งต่อการควบคุมระดับน้ำตาลในผู้ป่วยเบาหวานยังต้องศึกษาเพิ่มเติมในการศึกษาที่มีขนาดตัวอย่างมากเพียงพอ*