Association between hs-CRP and HbA1c in Overweight Type 2 Diabetic Female Patients

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Background and Objective: *High-sensitive C-reactive protein (hs-CRP) is associated with atherosclerosis. Previous studies have shown that hs-CRP is associated with insulin resistance, type 2 diabetes and higher HbA1c levels. As type 2 diabetes is often found in overweight women, the present study investigated the relationship between hs-CRP and HbA1c levels in such patients.*

Material and Method: *This was a retrospective study of type 2 diabetic patients in Rajavithi Hospital from January 2009 until June 2011. All the subjects were females aged 40 years or more who had body mass index (BMI) of more than 25 kilograms per square metre. The patients were examined and blood was collected in order to check hs-CRP and HbA1c levels.*

Results: *Data from 75 cases, classified the patients into 2 groups by their levels of hs-CRP and risk of coronary artery disease. Of the 75 patients, 35 had hs-CRP levels less than 1 mg/L, and the remaining 40 patients had hs-CRP levels of 1 mg/L or more, representing 46.67% and 53.33% respectively, and it was found that hs-CRP values correlated with HbA1c levels. The group with hs-CRP of less than 1 milligram per liter had a mean HbA1c of 7.36 $\pm$ 1.23%, while the group with hs-CRP of 1 mg/L or more had a mean HbA1c of 8.77 $\pm$ 1.78%, with statistical significance at p-value < 0.001.*

Conclusion: *In the present study of patients with type 2 diabetes, the authors found that hs-CRP levels correlated with HbA1c levels. Mean HbA1c levels were significantly higher in patients who had hs-CRP levels of 1 mg/L or more (p-value < 0.001). Other factors such as age, blood pressure, BMI, LDL-C, serum creatinine were not correlated with hs-CRP level.*

Keywords*: hs-CRP, HbA1c*

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C-reactive protein (CRP), a pentaglobulin protein, is stimulated by many cytokines such as interleukin 6, and tumor necrosis factors-α (TNF-α) in the acute phase reaction from inflammation or infection. In the past, the level of CRP that could be measured was between 10-1,000 mg/L. Nowadays, improved technology has enabled us to also measure high sensitive CRP (hs-CRP), and there is a correlation between hs-CRP and the risk factor of cardiovascular disease[1-3]. People with hs-CRP levels lower than 1 mg/L are classified as the lowest-risk group, 1-3 mg/L is a moderate-risk group and more than 3 mg/L is the highest-risk group. Hs-CRP levels are affected by many factors such as: age, sex, BMI, metabolic syndrome, smoking and blood pressure. Hs-CRP levels in type 2 diabetic patients are higher than in non-diabetic patients[4-6], and there is a positive correlation between hs-CRP and HbA1c[7]. Another study found that there was a positive correlation between CRP and the prevalence of microalbuminuria and glycemic control[8] but the CRP in that study was not hs-CRP. There are many factors which affect hs-CRP levels and the patients with diabetes are often overweight women. Before the present one, there had been no study of the correlation between glycemic control and hs-CRP levels in a specific group of female overweight type 2 diabetic patients.

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Material and Method

This was a retrospective study of overweight female type 2 diabetic patients at Rajavithi Hospital between January 2009 and June 2011. The present study was approved by the ethic committee of Rajavithi Hospital.

The primary research aim of the present study was to find correlations between hs-CRP and glycemic control in overweight female type 2 diabetic patients. The secondary research objective was to find correlations in the same group between hs-CRP and other risk factors including age, blood pressure, BMI, LDL-C and serum creatinine.

The inclusion criteria of the subjects in the present study were patients who were: non-smoking; overweight (BMI $\geq$ 25 kg/m^2); female; type 2 diabetic patients; and aged at least 40 years old to limit the effect of confounding factors of age, sex, smoking and BMI. The exclusion criteria were patients who had infection or CRP $\geq$ 10 mg/L.

For calculation of sample size, the authors used the Lemeshow et al formula

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 . (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

$\alpha = 0.05$, $\beta = 0.2$ and the authors also consulted the reference study of Safiullah et al[9] in which it was found that there were correlations between mean HbA1c in groups with low and high hs-CRP.

($\bar{x}_1, \bar{x}_2 = 6.4, 7.9$ and $SD_1^2, SD_2^2 = 1.98^2, 2.39^2$)

$n = (1.96 + 0.842)^2 \times (1.98^2 + 2.39^2)/(6.4\text{-}7.9)^2 = 33$ per group

The authors recorded the patients' age, BMI, medication, blood pressure, FPG, HbA1c, hs-CRP and LDL-C according to the protocol flow chart. The data were analyzed and presented by number, percentage, mean and SD, and Chi-square and t-test were used to find correlations.

Results

The authors examined 75 cases who met the inclusion criteria. The baseline characteristics of the patients in the present study are shown in Table 1. There were 35 patients (47%) in the low-hs-CRP group (hs-CRP < 1 mg/L) and 40 patients (53%) in the high-hs-CRP group (hs-CRP $\geq$ 1 mg/L). In the high-hs-CRP group, 28 were moderate-risk patients (hs-CRP 1-3 mg/L), and 12 were high risk patients (hs-CRP > 3 mg/L).

There was no statistical significance ($p < 0.05$) between the low-hs-CRP group and high-hs-CRP group in terms of age, comorbid disease, current medication, blood pressure, BMI, FPG, LDL-C or serum creatinine as shown in Table 2. The group with low hs-CRP had a lower mean FPG than the high-hs-CRP group (135.06 vs. 149.38 mg/dL), but no statistical significance ($p = 0.195$) was found. The group with low hs-CRP had a lower mean HbA1c than the high-hs-CRP group (7.36% vs. 8.77%), and these values were statistically significant ($p < 0.001$).

Fig. 1 shows that 76% of the patients in the group with good glycemic control (HbA1c < 7%) had hs-CRP < 1 mg/L compared to only 35% in the group with poor glycemic control ($p = 0.001$). Fig. 2 shows that the mean hs-CRP in the group with good glycemic control was 0.67 mg/L, but 2.05 mg/L in the group with poor glycemic control ($p < 0.001$).

Table 1. Baseline of the patients characteristic (n = 75)

Characters	
Patient characteristic	Number (%)
Sex	
Female	75 (100.0)
Current medications	
Statin	62 (82.7)
Aspirin	24 (32.0
ACE inhibitors or ARBs	62 (82.7)
Comorbid diseases	
hypertension	72 (96.0)
dyslipidemia	69 (92.0)
chronic renal failure	5 (6.7)
Age (years)	66.44 $\pm$ 9.91
Measurement	Mean $\pm$ SD
Blood pressure	
Mean systolic BP	138.91 $\pm$ 17.83
Mean diastolic BP	73.99 $\pm$ 10.24
BMI (kg/m^2)	28.98 $\pm$ 3.68
FBS (mg/dl)	142.69 $\pm$ 47.56
HbA1c (%)	8.11 $\pm$ 1.69
hs-CRP (mg/L)	1.66 $\pm$ 1.66
LDL (mg/dl)	103.53 $\pm$ 27.72
Serum creatinine (mg/dl)	1.05 $\pm$ 0.44

Values are represented as mean $\pm$ SD

Protocol flow chart

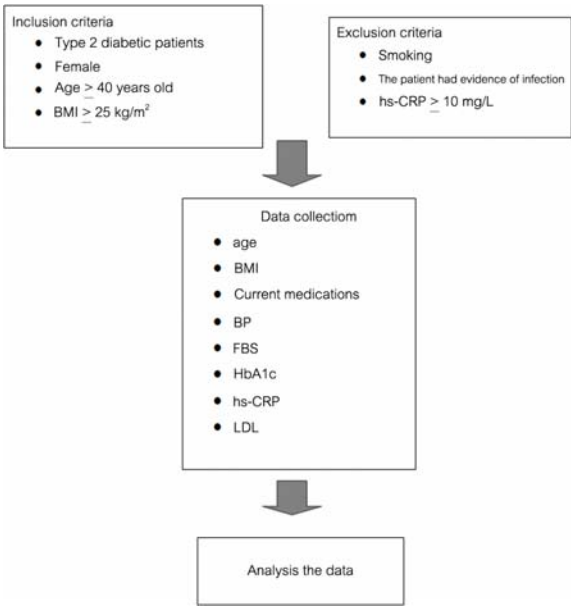

Table 2. Baseline characteristic of the patient by hs-CRP levels

Characters	hs-CRP < 1 mg/L (n = 35)	hs-CRP ≥ 1 mg/L (n = 40)	p-value
Current medications			
Statin (n = 62)	31 (50.0%)	31 (50.0%)	0.206
Aspirin (n = 24)	10 (41.7%)	14 (58.3%)	0.552
ACE inhibitors or ARBs (n = 62)	29 (46.8%)	33 (53.2%)	0.967
Comorbid diseases			
hypertension (n = 72)	32 (44.4%)	40 (55.6%)	0.097
Dyslipidemia (n = 69)	33 (47.8%)	36 (52.2%)	0.679
Chromic renal failure (n = 5)	1 (20.0%)	4 (80.0%)	0.364
Age (years)	66.03 ± 10.46	66.80 ± 9.5	0.739
Blood pressure (n = 75)			
Systolic blood pressure	138.57 ± 14.37	139.20 ± 20.56	0.880
Diastolic blood pressure	76.23 ± 10.33	72.03 ± 9.87	0.076
BMI (kg/m^2)	28.65 ± 3.82	29.28 ± 3.57	0.463
FBS (mg/dL)	135.06 ± 46.47	149.38 ± 48.07	0.195
HbA1c (%)	7.36 ± 1.23	8.77 ± 1.78	< 0.001*
LDL-C (mg/dL)	102.89 ± 23.63	104.10 ± 31.15	0.851
Serum creatinine (mg/dL)	0.96 ± 0.29	1.12 ± 0.53	0.115

Values are represented as n (%), mean ± SD, * = significance at p < 0.05

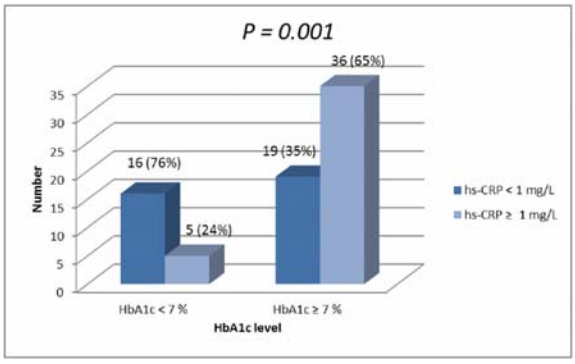

Fig. 1 The number of the patients with low and high hs-CRP in group of good and poor glycemic control

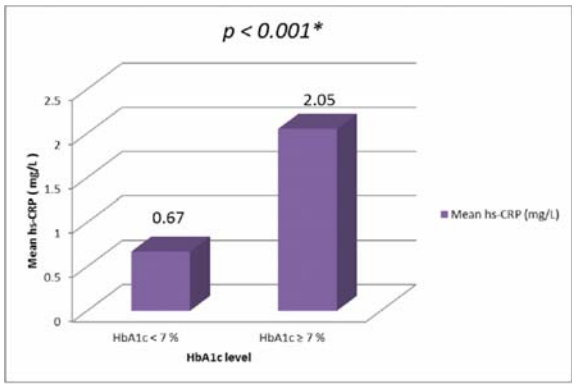

Fig. 2 Mean of hs-CRP in group with good and poor glycemic control

Discussion

The present study was conducted with non-smoking female overweight type 2 diabetic patients to evaluate the association of hs-CRP, which one of the independent cardiovascular risk factors, and glycemic control, and the authors found that there were correlations. The authors found that the group with good glycemic control had lower hs-CRP levels and a higher proportion of this group had hs-CRP < 1 mg/L. The group with low hs-CRP had a lower mean HbA1c than the group with high hs-CRP. With regard to our secondary research aim, the authors could not find any correlation between hs-CRP and other risk factors such as: age, comorbid disease, BMI and LDL-C because the subjects in the present study were all non-smoking overweight females. The present results confirm those of the previous studies which found that there was correlation between hs-CRP and glycemic control[8,10]. There were three limitations of the present study: first, it was a study of a specific group of overweight females and may not apply to other groups; second, measurement of hs-CRP was done only once and it has been suggested that the level of hs-CRP should be taken as the mean of two measurements; third, this was a retrospective study and the authors could not control others unknown risk factors. The

authors need more prospective studies to see the effect of treatment and to judge whether improved glycemic control will lower hs-CRP or not. A recent study found that improving glycemic control with lifestyle intervention found reduced CRP in obese subjects with type 2 diabetes[11]. However, the study was unable to conclude whether the effect of lifestyle intervention or the effect of lowering of glucose was the main cause of CRP reduction.

Potential conflicts of interest

None.

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ความสัมพันธ์ระหว่าง hs-CRP กับระดับของ HbA1c ของผู้ป่วยเพศหญิงที่มีโรคเบาหวานชนิดที่ 2 และมีภาวะน้ำหนักตัวเกิน

วีระศักดิ์ ศรินนภากร, วรางคณา วานิชกูล

ภูมิหลังและวัตถุประสงค์: *high-sensitive c reactive protein (hs-CRP) มีความสัมพันธ์กับการเกิดโรคหลอดเลือดแข็ง การศึกษาในอดีตพบว่า hs-CRP มีความสัมพันธ์กับภาวะดื้อต่ออินซูลิน, โรคเบาหวานชนิดที่ 2 และระดับ HbA1c ที่สูง เนื่องจากผู้ป่วยโรคเบาหวานมักจะพบในเพศหญิงที่มีน้ำหนักเกิน การศึกษานี้จึงได้ศึกษาถึงความสัมพันธ์ระหว่าง hs-CRP และระดับ HbA1c ผู้ป่วยดังกล่าว*

วัสดุและวิธีการ: *เป็นการศึกษาแบบวิจัยเชิงพรรณนาย้อนหลัง โดยกลุ่มผู้ป่วยที่ใช้ในการศึกษาทุกรายเป็นผู้ป่วยโรคเบาหวานชนิดที่ 2 ในโรงพยาบาลราชวิถี ในช่วงระหว่างเดือนมกราคม พ.ศ. 2552 จนถึงเดือนมิถุนายน พ.ศ. 2554 โดยเป็นผู้ป่วยเพศหญิงที่มีอายุตั้งแต่ 40 ปีขึ้นไป และมีดัชนีมวลร่างกายตั้งแต่ 25 ขึ้นไป โดยผู้ป่วยแต่ละรายได้ทำการตรวจร่างกาย และตรวจเลือดวัดระดับ hs-CRP และระดับ HbA1c แล้วนำข้อมูลมาวิเคราะห์เปรียบเทียบค่าความสัมพันธ์โดยใช้สถิติ chi-square และ t-test*

ผลการศึกษา: *จากข้อมูลตัวอย่าง 75 ราย สามารถจำแนกผู้ป่วยออกเป็น 2 กลุ่ม ตามระดับ hs-CRP โดยแบ่งตามความเสี่ยงต่อการเกิดโรคหัวใจและหลอดเลือดต่ำ ผู้ป่วย 35 ราย จาก 75 ราย มีระดับ hs-CRP ต่ำกว่า 1 มิลลิกรัมต่อลิตร และ 40 ราย มีระดับ hs-CRP ตั้งแต่ 1 มิลลิกรัมต่อลิตรขึ้นไป คิดเป็นร้อยละ 46.67 และ 53.33 ตามลำดับ และพบว่าค่าของ hs-CRP มีความสัมพันธ์กับ HbA1c คือ กลุ่มที่มีระดับ hs-CRP ต่ำกว่า 1 มิลลิกรัมต่อลิตร มีค่าเฉลี่ยของ HbA1c 7.36 $\pm$ 1.23 เปอร์เซ็นต์ ต่ำกว่ากลุ่มที่มีปัจจัยเสี่ยงต่อการเกิดโรคของระบบหัวใจและหลอดเลือดปานกลางถึงสูง คือ กลุ่มที่มีระดับ hs-CRP ตั้งแต่ 1 มิลลิกรัมต่อลิตรขึ้นไป ซึ่งมีค่าเฉลี่ยของ HbA1c 8.77 $\pm$ 1.78 เปอร์เซ็นต์ โดยมีนัยสำคัญทางสถิติที่ p-value < 0.001**

สรุป: *จากการศึกษาพบว่าระดับ hs-CRP ในผู้ป่วยโรคเบาหวานชนิดที่ 2 มีความสัมพันธ์กับระดับ HbA1c โดยกลุ่มที่มี hs-CRP ต่ำกว่า 1 มิลลิกรัมต่อลิตร จะมีค่าเฉลี่ยของ HbA1c น้อยกว่ากลุ่มที่มี hs-CRP ตั้งแต่ 1 มิลลิกรัมต่อลิตรอย่างมีนัยสำคัญทางสถิติ (p-value < 0.001*) ส่วนปัจจัยอื่นเช่น อายุ ความดันโลหิต ดัชนีมวลกาย ระดับไขมัน LDL-C และระดับค่าครีเอตินีน ไม่มีความสัมพันธ์กับระดับ hs-CRP*