Original Article

Association of High Sensitive C-Reactive Protein and Obesity in Thais

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Background: Obesity, a public health problem in many countries, was related to cardiovascular risk. High sensitive C-reactive protein (hs-CRP) was a predictor of cardiovascular disease (CVD) risk and elevated in inflammatory diseases.

Objective: To investigate the association between hs-CRP and obesity among Thais.

Materials and Methods: The present study was cross-sectional study. One hundred eleven adults were randomly recruited, and the anthropometric parameters were measured. Obesity indices, such as body mass index (BMI), body adiposity index (BAI), and waist to hip ratio (WHR) were calculated to estimate the obesity. Spearman's correlation was used to evaluate the association between hs-CRP and obesity indices. The subjects were divided into three CVD risk groups according to hs-CRP levels. The hs-CRP less than 1 mg/L (n=31), the hs-CRP 1 to 3 mg/L (n=54), and the hs-CRP more than 3 mg/L (n=26) determined the low, intermediate, and high CVD risk groups, respectively. One-way ANOVA was used to determine the significant differences of obesity indices among the low, intermediate, and high CVD risk groups.

Results: The present study showed a positive correlation between hs-CRP and obesity indices such as waist circumference ($p<0.001$, $r=0.416$), weight ($p=0.001$, $r=0.311$), hip circumference ($p<0.001$, $r=0.376$), WHR ($p=0.024$, $r=0.214$), BMI ($p<0.001$, $r=0.383$), and BAI ($p<0.001$, $r=0.334$). The results demonstrated that values of all obesity indices were elevated in intermediate and high CVD risk groups. BMI, waist circumference, and WHR expressed significant differences among low, intermediate, and high-risk groups ($p<0.05$). In addition, hs-CRP was significantly elevated in obese people compared with non-obese people.

Conclusion: The hs-CRP positively correlated with obesity indices indicating the association between high level of hs-CRP and obesity.

Keywords: Cardiovascular disease, High sensitive C-reactive protein, Obesity, Obesity indices

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The prevalence of obesity has markedly increased in industrialized and developing countries worldwide[1,2]. The World Health Organization (WHO) reported that 1.9 billion adults were overweight and over 650 million were obese in 2016. Obesity is the chronic disease leading to arthritis, hypertension, heart disease, stroke, cancer, and diabetes[1]. Abdominal obesity is the most important factor of diabetes and cardiovascular disease (CVD) resulting in morbidity and mortality[2]. About 8.7% of all deaths in United Kingdom resulted from obesity[1]. The most common tool used to assess and classify obesity is body mass index (BMI), which relates weight to height. Other anthropometric parameters such as waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR) have been used to determine obesity[2].

C-reactive protein (CRP) is a plasma protein synthesized by liver. It is a sensitive inflammatory marker that increases in non-specific acute-phase inflammations, infection, and tissue damage. CRP was modulated by mediators of the inflammatory cascade, such as interleukin 6. The level of CRP is elevated in several diseases, for example, CVD,

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metabolic syndrome, diabetes, and some types of cancers[3,4]. An increase of CRP level correlated with high-risk of coronary heart disease (CHD) and peripheral vascular disease in diabetes[5]. In addition, CRP levels relate to cardiovascular risk factors, such as BMI, WC, blood pressure, plasma glucose, total cholesterol (TC), triglycerides, and TC/high-density lipoprotein cholesterol (HDL-C) in Indian population[3]. However, research on association between CRP and obesity indices need more study in Thai population. Therefore, the association between high sensitive C-reactive protein (hs-CRP) levels and obesity parameters among Thais was examined in the present study.

Materials and Methods

Study participants

The present cross-sectional study was performed around Lak-Hok Sub-district, Muang District, Pathum Thani Province in July 2017. One hundred and eleven participants were randomly recruited to the Medical Technology Clinic, Rangsit University in the project of Medical Technology for community. Most participants in the present project were female. The written informed consent was obtained from each participant. The participants who have acute infection, autoimmune diseases, severe degenerative diseases, and current use of antibiotic were excluded. The present study was approved by the Ethical Committee of Research Institute of Rangsit University (RSEC 11/2560).

Demographic information

Demographic information including age, sex, systolic and diastolic blood pressure, and history of illness was recorded. Body weight (kg), height (cm), WC (cm), and hip circumference (cm) of the subjects were measured. WHR was calculated by dividing WC (cm) by hip circumference (cm). BMI was calculated by dividing weight (kg) by the square of the height (m). The body adiposity index (BAI) was calculated as BAI = [hip circumference (cm)/height (m)$^{1.5}$] – 18[6].

Biochemical measurements

Heparinized blood was collected and centrifuged at 3,000 rpm for 10 minutes. The plasma was subjected to an automate analyzer (Cobas INTEGRA 400 plus, Roche, Switzerland) for clinical measurements including glucose (mg/dL), TC (mg/dL), HDL-C (mg/dL), triglyceride (mg/dL), and low-density lipoprotein cholesterol (LDL-C) (mg/dL). The hs-CRP was measured by particle enhanced immunoturbidimetric assay using Cobas 6000 automate analyzer (Roche, Switzerland). The monoclonal anti-CRP antibody coated on latex particles was used to agglutinate human CRP in plasma. The precipitate is determined by turbidimetrically. The absorbance was positively correlated with the concentration of CRP. The measuring range is 0.15 to 20.00 mg/L. The hs-CRP was grouped by the Centers for Disease Control and Prevention or the American Heart Association (CDC/AHA) cut off points following the CVD risk[7].

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics software, version 23 (IBM Corp., Armonk, NY, USA). Mean of several parameters compared between male and female was analyzed by two independent samples t-test in case of normal distribution (Table 1). Non-normal distribution data were analyzed by Mann-Whitney U test (Table 1). Spearman's correlation was used to analyze the correlation between hs-CRP and obesity indices (Table 2). The statistical differences of adiposity indices in each CVD risk group were determined by One-way ANOVA test (Table 4). The statistical significance was indicated by p-value of less than 0.05.

Results

Participant characteristics

The demographic information of the 111 participants is shown in Table 1. The subjects were grouped by sex (22 male and 89 female) and the mean of each parameter was compared between male and female. The obesity indices including weight, BMI, WC, hip circumference, WHR, BAI, and hs-CRP were analyzed. Overall, male and female had significant difference in parameters of height, weight, WHR, BAI, and HDL-C. The mean of BAI, which reflected the % body fat, was significantly different in female compared to male. The other obesity parameters were not significantly different between male and female. Although, the level of hs-CRP in male was higher than female, the statistics showed no significant difference between these two groups.

The hs-CRP correlated with obesity indices

The hs-CRP was measured in all participants and statistical analysis was performed to investigate the relation of obesity indices and hs-CRP (Table 2). Interestingly, all obesity indices including weight, WC, hip circumference, WHR, BMI, and BAI expressed the positive correlation with hs-CRP

Table 1. Participant characteristics

Parameters	All (n=111) Mean±SD	Female (n=89) Mean±SD	Male (n=22) Mean±SD	p-value
Age (years)	59.25±8.49	58.73±7.98	61.36±10.23	0.337
Height (cm)	156.22±6.76	154.37±5.27	163.68±7.07	<0.001***
Weight (kg)	61.38±9.53	59.88±8.71	67.46±10.45	0.001**
BMI (kg/m^2)	25.13±3.43	25.12±3.40	25.18±3.63	0.943
Waist circumference (cm)	88.23±9.09	87.55±9.05	91.00±8.91	0.111
Hip circumference (cm)	97.79±7.10	98.16±7.12	96.32±7.00	0.279
WHR	0.90±0.06	0.89±0.06	0.95±0.06	0.001**
BAI	32.24±4.73	33.27±4.33	28.11±4.04	<0.001***
Systolic BP (mmHg)	138.95±18.23	137.78±18.71	143.73±15.60	0.171
Diastolic BP (mmHg)	80.09±11.17	79.29±11.31	83.32±10.21	0.131
Total cholesterol (mg/dL)	209.25±47.35	213.03±48.54	193.95±39.54	0.091
HDL-C (mg/dL)	57.22±15.96	59.33±16.08	48.70±12.49	0.005**
hs-CRP (mg/L)	2.68±4.35	2.36±2.27	3.96±8.67	0.959

SD=standard deviation; BMI=body mass index; WHR=waist to hip ratio; BAI=body adiposity index; BP=blood pressure; HDL-C=high-density lipoprotein cholesterol; hs-CRP=high sensitive C-reactive protein

Statistically significant, * p<0.05, ** p<0.01, *** p<0.001

Table 2. Correlation between obesity indices and hs-CRP

	hs-CRP (n=111)	
	p-value	Correlation coefficient
Waist circumference (cm)	<0.001***	0.416
Weight (kg)	0.001**	0.311
Hip circumference (cm)	<0.001***	0.376
WHR	0.024*	0.214
BMI (kg/m^2)	<0.001***	0.383
BAI	<0.001***	0.334

BMI=body mass index; WHR=waist to hip ratio; BAI=body adiposity indexhs-CRP=high sensitive C-reactive protein

Statistically significant, * p<0.05, ** p<0.01, *** p<0.001

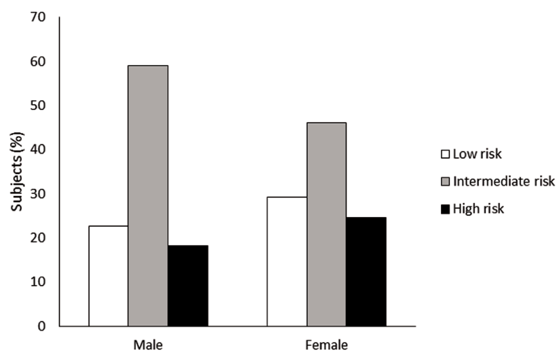

Figure 1. The percentage of male and female categorized by CVD risk.

and p-values were less than 0.05. The correlation coefficients (CC) were 0.214 for WHR, 0.311 for weight, 0.334 for BAI, 0.376 for hip circumference, 0.383 for BMI, and 0.416 for WC. Therefore, high level of hs-CPR may be involved in high obesity indices and reflect the obesity.

The association of obesity factors and CVD risk

The hs-CRP was grouped by CDC/AHA cut off points following the CVD risk. Low, intermediate, and high CVD risks were characterized by hs-CRP levels which are lower than 1 mg/L, 1 to 3 mg/L, and more than 3 mg/L, respectively. The percentage of each CVD risk group was categorized by sex (Figure 1). The highest percentage of male and female, was intermediate risk group (male 59.1%, female 46.1%). The second and third ranks in each group were low (male 22.7%, female 29.2%), and high (male 18.2%, female 24.7%) CVD risk, respectively. The percentage of intermediate risk in male was higher than in female. In contrast, low and high-risk group in female were higher than in male. The participants were divided into three groups according to hs-CRP level described above. Most subjects had hs-CRP level around 1 to 3 mg/L and were in the intermediate risk group. Thirty-one participants were in the low-risk group (hs-CRP of less than 1 mg/L), and 26 subjects were in the high-risk group (more than 3 mg/L). The mean ± standard

Table 3. Obesity indices related to CVD risk group according to hs-CRP levels

Obesity indices	Low risk (<1 mg/L) (n=31) Mean±SD	Intermediate risk (1 to 3 mg/L) (n=54) Mean±SD	High risk (>3 mg/L) (n=26) Mean±SD
BAI	30.41±4.00	32.12±4.63	34.69±4.84[ab]
BMI (kg/m^2)	23.40±2.99	25.07±3.00[a]	27.33±3.63[ab]
Weight (kg)	57.36±8.30	61.65±9.21[a]	65.62±9.91[a]
Waist circumference (cm)	82.52±9.04	89.07±7.89[a]	93.31±8.02[ab]
Hip circumference (cm)	94.55±5.80	97.94±6.68[a]	101.35±7.78[a]
WHR	0.87±0.08	0.91±0.06[a]	0.92±0.04[ab]

SD=standard deviation; BMI=body mass index; WHR=waist to hip ratio; BAI=body adiposity index

[a] p<0.05 vs low risk group; [b] p<0.05 vs. intermediate

Table 4. The hs-CRP and obesity indices in non-obese and obese people categorized by BMI

Parameters	Non-obese (≤24.99 kg/m^2) (n=58) Mean±SD	Obese (≥25.00 kg/m^2) (n=53) Mean±SD	p-value
hs-CRP	1.76±1.60	3.68±5.93	0.001**
BAI	29.84±3.73	34.87±4.32	<0.001***
Weight (kg)	55.00±5.97	68.36±7.61	<0.001***
Waist circumference (cm)	82.48±7.19	94.53±6.39	<0.001***
Hip circumference (cm)	93.12±5.23	102.91±5.07	<0.001***
WHR	0.89±0.07	0.92±0.05	0.007**

SD=standard deviation; BMI=body mass index; WHR=waist to hip ratio; BAI=body adiposity index; BP=blood pressure; HDL-C=high-density lipoprotein cholesterol; hs-CRP=high sensitive C-reactive protein

Statistically significant, ** p<0.01, *** p<0.001

deviation (SD) of obesity indices was shown in Table 3. The results showed that the mean of weight, WC, hip circumference, WHR, BMI, and BAI was increased in intermediate and high-risk comparing with low-risk group. Statistically significant differences between groups were determined by One-way ANOVA. BAI was significantly higher in the high-risk group than in the intermediate and low-risk groups. BMI, WC, and WHR of high-risk group were significantly higher than in the intermediate and low-risk groups. Weight and hip circumference of the high and intermediate risk groups were highly significant compared to the low-risk group. All parameters except BAI were significantly higher in the intermediate risk group than in the low-risk group (p<0.05).

High obesity indices and hs-CRP in obese group

The participants were grouped into two groups by BMI according to criteria of Asian people[8]. The first group was non-obese having a BMI of 24.99 kg/m^2 or less. The second group had a BMI of 25.00 kg/m^2 or more and were categorized as obese. These two groups were compared with obesity parameters and hs-CRP. The p-values from Mann-Whitney U test are shown in Table 4. The average values of all parameters including hs-CRP, BAI, weight, WC, hip circumference, and WHR of the obese group were significantly higher than in the non-obese group.

Discussion

To the authors' knowledge, the present study is the first to report the association between hs-CRP and obesity indices among Thais. CRP is a sensitive inflammatory marker that increases in non-specific acute-phase inflammations, infection, and tissue damage. The elevated rate of CRP is 100-fold higher than basal level and decreased to baseline after 7 to 12 days[5]. The CRP increases rapidly to above 5 mg/L after six hours of stimulation and is the highest at 48 hours. The level of CRP remains stable in healthy and diseases until the stimulation stops[9]. Plasma CRP concentration directly reflects the intensity of the pathological process stimulating CRP production[9].

In the present study, 111 participants were recruited in Pathum Thani Province. General characteristics were similar in male and female.

Some parameters were significantly different including height, weight, WHR, BAI, and HDL-C. Height, weight, and WHR were higher in male than in female. In contrast, BAI and HDL-C in female were higher than in male indicating that body fat of female was higher than male. The present study's result was similar with previous study(10,11). The gender difference in HDL-C level may be explained by the effect of estrogen(11). The higher hs-CRP level together with lower HDL-C level suggested that males were prone to CVD.

Obesity indices including WC, weight, hip circumference, WHR, BMI, and BAI were used to characterize the obesity. The present study demonstrated that these parameters associated with hs-CRP with positive correlation and statistical significance ($p<0.05$). The present study's results were consistent with the previous studies showing that hs-CRP positively correlated with BMI, WC, plasma glucose, TC, TC/HDL-C, triglycerides, and blood pressure(3,12,13).

The subjects were grouped using CRP levels to determine the risk levels of CVD. The results demonstrated that most subjects were 1 to 3 mg/L of CRP indicating intermediate risk of CVD. The percentage of high-risk of CVD and the value of BAI in female were higher than male. All obesity parameters of the high-risk group were higher than of the intermediate and low-risk groups indicating that obesity factors were clearly associated with the risk of CVD.

Increasing of hs-CRP in obese patients could be explained by the effect of inflammatory response. Obese patient had a chronic low-grade inflammation; therefore, interleukin (IL)-6 was overexpressed(14). IL-6 was released from an important source, adipose tissue. In obese state, the expanding adipose tissue may provide a major source of high IL-6(15). Hence, CRP is released from the liver due to stimulation by IL-6(16).

BMI was used to determine obesity several years ago. The range of BMI was different in each ethnic group. Therefore, the authors cannot use the same criteria in different ethnic groups. The inaccuracy may occur in some people who had increase lean body mass such as athletes because BMI was calculated from body weight and height(17,18). Due to some limitations of BMI, Bergman et al(6) suggested that BAI be a better index of body adiposity. BAI was calculated by only height and hip circumference without using a mechanical or electronic measurement of body weight. Height of adults is constantly increasing the reliability of % adiposity(6). However, the measurement of hip circumference may introduce some error of BAI estimation. The sensitive biomarker to determine obesity remains to be investigated. The authors' results showed that CRP levels strongly correlated with obesity suggesting the same marker used to evaluate obesity and CVD risk. In addition, Stępień et al reported that hs-CRP level was more elevated in obese people than in normal weight or overweight subjects(19), which is consistent with the present study results. Therefore, CRP may be used as the biomarker for obesity parallel with obesity indices such as BMI or BAI to predict the CVD risk.

However, the authors' findings about correlation between hs-CRP and obesity had some limitations. The confounders including pre-existing CVD subjects, diabetes, and post-menopausal women were not excluded from the present study. These factors may affect the hs-CRP level and should be studied further.

Conclusion

The hs-CRP strongly associated with obesity indices including weight, WC, hip circumference, WHR, BMI, and BAI. High CVD risk group categorized by hs-CRP has higher obesity indices than other CVD risk groups suggesting that the obese people were susceptible to CVD.

What is already known on this topic?

Prevalence of obesity has increased worldwide, including Thailand. Few studies reported the relationship between hs-CRP and obesity in Thais.

What this study adds?

The study found a positive correlation between hs-CRP level and obesity indices such as BMI and BAI in Thais and support a same correlation as in other countries.

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Conflicts of interest

The authors declare no conflict of interest.

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