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Research Article

HIGH SENSITIVE C-REACTIVE PROTEIN AND ITS RELATIONSHIP WITH OTHER CARDIOVASCULAR RISK VARIABLES IN OBESE, OVERWEIGHT AND HEALTHY INDIVIDUALS

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ABSTRACT

Objective: More than 50% of the world's population is considered overweight and being overweight is associated with several comorbidities such as Type 2 diabetes mellitus, hypertension, cardiovascular diseases, dyslipidemia, respiratory diseases, osteoarthritis, and depression. Therefore, in this study, we have estimated the high sensitive C-reactive protein (hs-CRP) levels in obese, overweight, and normal body mass index (BMI) individuals and whether there was any relationship between hs-CRP and other risk factors of the cardiovascular system such as serum total cholesterol (TC) and other lipids.

Methods: A total of 150 participants, divided into three groups. Group I - 50 participants with normal BMI (18–22.99 kg/m^2), Group II - 50 participants who were overweight (BMI = 23–24.99 kg/m^2), and Group III - 50 who were obese (BMI ≥25 kg). We measured fasting plasma glucose, postprandial plasma glucose, serum TC, triacylglycerol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and hs-CRP.

Results: Obese individuals had increased hs-CRP compared with control (Group I) and overweight (Group II) groups. hs-CRP positively correlated with BMI and lipid profile.

Conclusion: Elevated hs-CRP was associated with cardiovascular risk factors in overweight and obese individuals. This high-risk group should be targeted for therapeutic lifestyle modifications to prevent further complications.

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

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INTRODUCTION

The rapidly growing rate of obesity is a severe health problem [1]. The basic cause of this problem is mostly due to the imbalance between energy intake and expenditure which induces an excessive accumulation of body fat [2]. Obesity is a chronic disorder prevalent in both developed and developing countries. More than half of the world's population is considered overweight and being overweight is associated with several comorbidities such as Type 2 diabetes mellitus, cardiovascular diseases (CVD), hypertension, dyslipidemia, respiratory disease, osteoarthritis, and depression [3]. It has been shown that pro-inflammatory molecules contribute to the development of complications in obesity [4]. These conditions are operationally defined by a surrogate measurement that correlates with body fat, body mass index (BMI), defined as body weight (kg) divided by the square of height (m^2).

BMI is the most commonly used method for describing obesity and assessing the risk for obesity-related diseases [5]. CVD is now recognized to be a process involving inflammatory processes, and serum inflammatory markers are considered to be important for the evaluation of cardiovascular risk [6]. It is possible that the relationship between CVD risk and obesity is linked to the increased inflammatory milieu [7]. High sensitive C-reactive protein (hs-CRP), an inflammatory marker, has been considered as an important indicator of cardiovascular risk [8]. Obesity has been associated with a chronic, low-level activation of the acute-phase response [9,10], suggesting that it is an "inflammatory disease." It is still not clear whether inflammatory parameters are markers or mediators of insulin resistance and CVD. The increased production of cytokines and acute-phase response proteins, such as hs-CRP, which occurs in obesity, is related to insulin resistance, endothelial dysfunction, and atherosclerosis [11]. CRP is a member of the pentraxin family of proteins. It is an acute phase reactant synthesized mainly by the liver in response to stimulation by pro-inflammatory cytokines and adipocytes [12]. Serum CRP levels are elevated in response to acute infections, inflammatory conditions, and trauma. In these clinical situations, the serum CRP levels rise rapidly generally beyond 10 mg/dl with a concomitant elevation of erythrocyte sedimentation rates [13].

We planned the present study to investigate a state of chronic low-grade systemic inflammation by measuring serum hs-CRP levels in overweight and obese individuals and comparing them with a group of age and sex matched controls with normal BMI.

METHODS

This cross-sectional study included a total of 150 (group 1=50 normal BMI, group 2=50 overweight, and group 3=50 obese) individuals, aged between 18 and 54 years, who have attended the Master health Checkup Programme of SRM Medical College Hospital and Research Centre between June 2016 and March 2017 and met the research criteria. The study was approved by the Institutional Ethical Committee of SRM Medical College Hospital and Research Centre, and written informed consent was obtained from all the participants (IEC no -957/IEC/2016).

The important confounding variables such as diabetes mellitus, hypertension, smoking, alcohol intake, acute or chronic infections, and history of drug intake were excluded. According to consensus statement, normal BMI is 18.0–22.9 kg/m^2, overweight is 23.0–24.9 kg/m^2, and obesity is ≥25 kg/m^2 [14].

We have included three groups based on the BMI Group 1 (Normal) BMI =18.0–22.9 kg/m^2, Group 2 (Overweight) BMI=23.0–24.9 kg/m^2, and Group 3 (Obese) BMI ≥25 kg/m^2 [15].

Anthropometric measurements

BMI, calculated as weight (kg) divided by height (m^2), was used as a measure of overall obesity. Anthropometric measurements such as body weight and height were measured by the same observer in the morning. Body height and weight were measured using a stadiometer and a standardized scale, respectively.

Biochemical parameters

Two ml blood was collected in a fluoride oxalate vacutainer for glucose measurement and measured immediately using automated chemistry analyzer (BECKMAN COULTER AU 480). Five ml blood was collected in a plain vacutainer. Serum was separated after centrifugation at 3,000 RPM for 10 min and lipid profile parameters, namely total cholesterol (TC) (cholesterol oxidase method), triglycerides (glycerol phosphate oxidase peroxidase), low-density lipoprotein cholesterol (LDL-C direct method), and high-density lipoprotein cholesterol (HDL-C direct method) were measured immediately using automated chemistry analyzer (BECKMAN COULTER AU 480). Postprandial sample collected for plasma glucose (PPG) measurement. Cholesterol/HDL-C and LDL-C/HDL-C ratios were calculated by subdividing TC and LDL-C, respectively, by HDL-C. 0.5 ml of serum sample stored in a deep freezer at −20° for 2 months for estimation of serum hs-CRP. Estimation of serum hs-CRP was carried out by turbidimetry latex-high sensitivity kit in OLYMPUS AU400.

Statistical analysis

Statistical comparisons were carried out by Student's t-test and one-way ANOVA tests. Correlations were done by calculating Pearson's correlation coefficient. This was conducted using IBM SPSS Statistics 20. Simple descriptive statistics (mean and Standard Deviation) were used to describe the observed variation in lipid profile, hs-CRP, fasting plasma glucose (FPG), and PPG between the groups under the study.

RESULTS AND DISCUSSION

The total number of subjects included in this analysis was 150, of which 50 had BMI ≥25 kg/m^2 (obese), 50 had BMI in the range of 23–24.9 kg/m^2 (overweight), and 50 participants were age and sex matched with normal BMI (18–22.9 kg/m^2) which formed the control group.

Table 1 shows the measured parameters of the three study groups.

The differences in serum hs-CRP levels between the three groups tested using one-way ANOVA method were found to be statistically significant ([F=88.070], p≤0.00001). The difference between the levels of BMI, FPG, PPG, TC, triacylglycerol (TGL), LDL-C, and very LDL-C tested by one-way ANOVA method was also found to be statistically significant across the three groups (Tables 2 and 3).

There was a positive correlation between hs-CRP levels and BMI in obese and overweight individuals (Figs. 1-3).

In this study, we showed that hs-CRP levels were higher in obese and overweight individuals when compared with age- and sex-matched normal BMI individuals. hs-CRP was positively correlated with BMI, TC, LDL-C, and TGL and was negatively correlated with HDL-C. It is considered that clustering of metabolic abnormalities presents synergistic effects on cardiovascular complications beyond the sum of effects of individual abnormalities [16].

Serum levels of hs-CRP have been shown to correlate with future risk of cardiovascular events since an inflammatory component has been well recognized in the atherosclerotic process [17]. Vino *et al.* reported that the correlation of BMI or waist circumference with hs-CRP concentration has also been observed [18,19]. In women with polycystic ovary syndrome (PCOS), the levels of hs-CRP, apolipoprotein B, and waist-to-hip ratio were significantly elevated when compared with controls. Screening with hs-CRP and apolipoprotein B may provide a better risk assessment in patients with PCOS [20].

Perceived obesity comorbidity of respondents revealed in this study that majority knew obesity can lead to heart problems, hypertension, and diabetes. The findings of this study can provide baseline data for monitoring the effectiveness of national programs for the prevention and control of obesity in Malaysia [21]. Dutta *et al.* found that overweight patients significantly took dominance in a low-risk category and there was no significant correlation between AIP, TC, HDL, LDL, TG, and BMI [22].

hs-CRP was positively associated with BMI, WHR, LDL, TC, TG, and PCOS status and was negatively associated with HDL-C [23]. In our study, we found that the difference between the levels of TC, TGL, LDL-C, and VLDL-C was also found to be statistically significant among the three groups.

Subjects who had elevated levels of both leptin and hs-CRP belonged to the highest risk of developing metabolic syndrome [24]. Cutoff

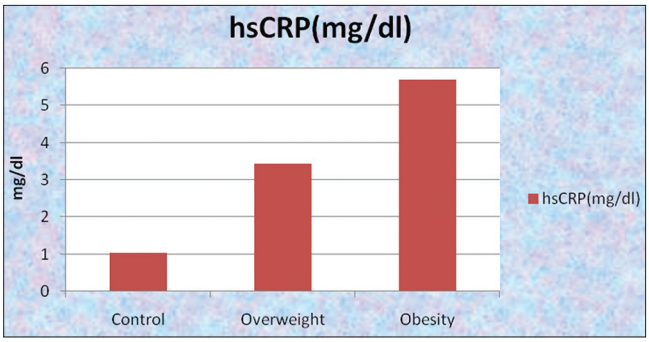

Fig. 1: Mean values of high sensitive C-reactive protein (mg/dl) of the study groups obese, overweight, and healthy

Table 1: Mean±standard deviation of measured parameters of the study groups

Parameter	Group I	Group II	Group III
	Control (n=50) Mean±SD	Overweight (n=50) Mean±SD	Obese (n=50) Mean±SD
BMI (kg/m^2)	20.16±1.5	23.67±0.57	30.02±4.27
hsCRP (mg/dl)	1.04±0.63	3.43±0.84	5.69±2.85
FPG (mg/dl)	95±11	94±14	104±13
PPPG (mg/dl)	111±15	111±16	123±14
TC (mg/dl)	155±18	161±23	192±35
TGL (mg/dl)	113±28	145±51	205±65
HDL-C (mg/dl)	41±9	41±5	38±6
LDL-C (mg/dl)	91±18	91±26	113±34
VLDL-C (mg/dl)	23±6	29±10	41±13
TC/HDL-C	3.98±1.02	4 0.0±7.0	5.18±1.17
LDL-C/HDL-C	2.39±0.88	2.27±0.7	3.06±1.04

BMI: Body mass index, hs-CRP: High sensitive C-reactive protein, TC: Total cholesterol, TGL: Triacylglycerol, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, VLDL-C: Very low-density lipoprotein cholesterol

Table 2: Comparison of biochemical parameters between the three groups using one-way ANOVA

Parameters	Sum of squares	df	Mean square	F value	p value
hsCRP (mg/dl)					
Between groups	543.8648	2	271.9324	88.070	<0.00001
Within groups	453.8883	147	3.0877		
Total	997.7531	149			
FPG (mg/dl)					
Between groups	3324.36	2	1662.18	10.68641	<0.000046
Within groups	22864.6	147	155.5415		
Total	26188.96	149			
PPPG (mg/dl)					
Between groups	4711.7733	2	2355.8867	10.19435	<0.000071
Within groups	33971.3	147	231.0973		
Total	38683.0733	149			
TC (mg/dl)					
Between groups	39586.4133	2	19793.2067	28.10343	<0.00001
Within groups	103531.88	147	704.2985		
Total	143118.2933	149			
TGL (mg/dl)					
Between groups	221710.6533	2	110855.3267	43.27248	<0.00001
Within groups	376584.18	147	2561.7971		
Total	598294.8333	149			
HDL-C (mg/dl)					
Between groups	294.28	2	147.14	3.02635	<0.0515
Within groups	7147.08	147	48.6196		
Total	7441.36	149			
LDL-C (mg/dl)					
Between groups	15627.1301	2	7813.5651	10.83389	<0.000041
Within groups	106018.6632	147	721.2154		
Total	121645.7933	149			
VLDL-C (mg/dl)					
Between groups	8868.4261	2	4434.2131	43.27248	<0.00001
Within groups	15063.3672	147	102.4719		
Total	23931.7933	149			
TC/HDL-C (mg/dl)					
Between groups	47.0434	2	23.5217	24.22644	<0.00001
Within groups	142.7237	147	0.9709		
Total	189.7671	149			
LDL-C/HDL-C (mg/dl)					
Between groups	18.2146	2	9.1073	11.51282	<0.00001
Within groups	116.2855	147	0.7911		
Total	134.5001	149			

p<0.05 Considered statistically significant. BMI: Body mass index, hs-CRP: High sensitive C-reactive protein, TC: Total cholesterol, TGL: Triacylglycerol, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, VLDL-C: Very low-density lipoprotein cholesterol

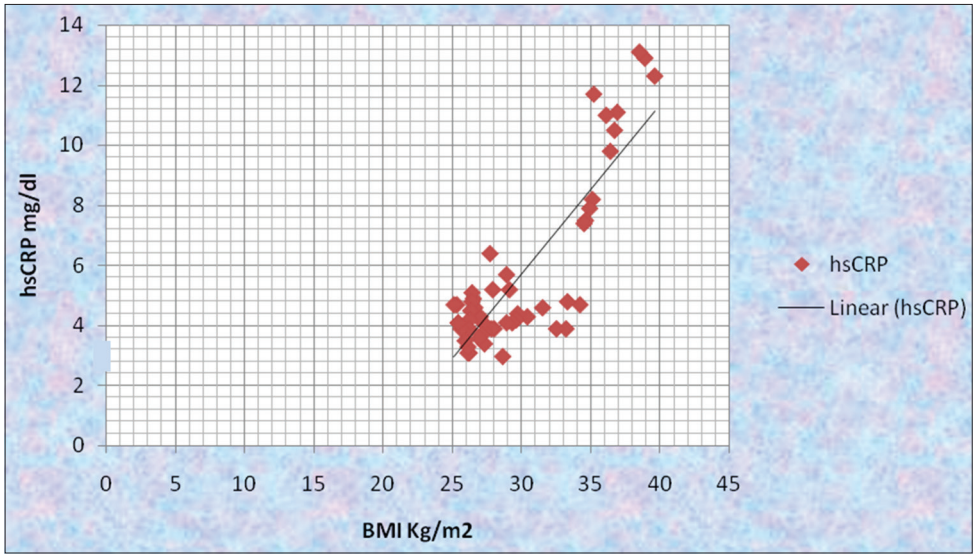

Fig. 2: Correlation of body mass index and high sensitive C-reactive protein (mg/dl) in obesity group

Table 3: Correlation between hs-CRP and lipid parameters among the three groups

Parameters	Controls (r value)	Overweight (r value)	Obese (r value)
BMI hsCRP	0.291	0.525	0.855
TC hsCRP	0.168	0.035	0.209
TGL hsCRP	0.396	0.151	0.748
HDL hsCRP	- 0.163	0.068	0.097
LDL hsCRP	0.129	0.180	0.192

BMI: Body mass index, hs-CRP: High sensitive C-reactive protein, TC: Total cholesterol, TGL: Triacylglycerol, LDL: Low-density lipoprotein, HDL: High-density lipoprotein

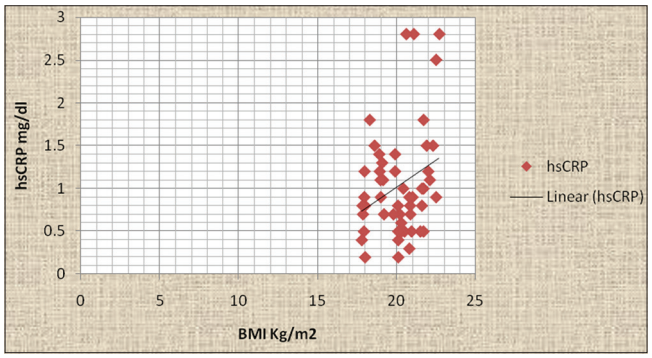

Fig. 3: Correlation between body mass index (BMI) and high sensitive C-reactive protein (mg/dl) in normal BMI group

limits >3 mg/dl in Hs-CRP levels indicate low-grade inflammation, which, in turn, might be a prognostic marker for further cardiovascular events [25]. The expansion of the adipose tissue leads to the altered production of pro-inflammatory molecules and results in low-grade inflammation. The increase in hs-CRP levels indicates a state of low-grade inflammation in the obese group [26].

Hak *et al.* [27] found that CRP was strongly related to BMI and the waist and hip circumferences separately; however, after adjustment for BMI, waist circumference was still related to CRP, whereas hip circumference was not.

There was a close relationship between hs-CRP and cardiovascular risk factors such as BMI, LDL-C, TC, HDL-C, and TGL. Limitations of this study are smaller sample size, and a prospective study is required to stratify the risk category among obese.

CONCLUSION

Our result suggests a strong correlation between indices of adiposity and elevated hs-CRP levels. Serum hs-CRP is an inexpensive, simple tool to predict cardiac risk in apparently healthy individuals at an early stage. Elevated hs-CRP was associated with cardiovascular risk factors in both overweight and obese individuals. This high-risk group should be targeted for therapeutic lifestyle modifications to prevent further complications. Screening of these apparently healthy individuals with the adjuvant novel biomarker hs-CRP will help in global cardiovascular risk assessment.

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AUTHOR'S CONTRIBUTION

None.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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