Section: Physiology

Original Research Article

PREDICTIVE VALUE OF HIGH SENSITIVE "C" - REACTIVE PROTEIN IN OBESE SUBJECTS

R. Hemavathy[1], K. Parveen Bobby[2], K. Soundariya[3], M. Jansi Rani Shivasubramaniam[4]

[1,2]Senior Assistant professors of Physiology at Government Vellore Medical College – Vellore, India.
[3]Professor of Physiology at Sri Manakula Vinayagar Medical College – Pondy, India.
[4]Professor & HOD of Biochemistry at Sri Danalakshmi Srinivasan Medical College – Perambalur, India.

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Corresponding Author:
Dr. R.Hemavathy,
Email: rhbnithin@gmail.com.

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Abstract

Background: Obesity is primarily considered to be a disorder of energy balance, and it has recently been suggested that some forms of obesity are associated with chronic low-grade inflammation. Obesity is a chronic, multifactorial and complex disease which poses a major public health issue increasing the risk of non - -communicable diseases like, Type -2-DM, Cardiovascular diseases, Hyperlipidemia, Hypertension etc. **Objectives:** The present study aims to emphasize the burden of obesity in inflammation by associating with elevated levels of hs CRP in adults. **Materials and Methods:** The study was a Hospital based cross sectional study including 20 obese individuals in the age group of 17-30 years,(8 males and 12 females)with BMI > 30 were included. Other systemic diseases were excluded. Assessment was done by Weight, Height, BMI by Quetelet index and measurement of hs CRP by Immunoturbidometer. The results were tabulated and analysed. **Results:** Total of 20 obese subjects were included of which 8 were males and 12 were Females. In obese subjects hs-CRPwas elevated significantly. The level of hs-CRP was proportionally elevated in relation to BMI in obese subjects. **Conclusion:** Elevated hs-CRP levels in obese individuals indicates a proinflammatory state. This further concludes a risk for metabolic and cardiovascular manifestations in obese individuals.

INTRODUCTION

Obesity is defined as a state of being overweight with excess body fat resulting in a significant impairment of health in a person. The most widely used method to gauge obesity is Quetelet index which is [weight (kg) / height (m^2)]. BMI of 30 is the most commonly used threshold for obesity in both men and women.[1] A data from National Health and Nutritional Examination survey (NHANES) shows that the percentage of American adult population with BMI > 30 has raised from 14.5 % to 30.5 %.[1] Approximately 55 % of adults in the united States are overweight, and nearly 22 % of adults are obese.[2]

Obesity is a long term disease having many serious consequences for health and it is a leading cause of preventable death in united states.[3] Obesity has become so common in developed and developing nations that presently it replaces undernutrition and infectious diseases as the most significant contributor to ill health.[4] Few decades before, obesity was considered as an indication of wealth and health or maximally as a cosmetic problem. But, now it has become an epidemic that threatens global well-being even in growing children and adolescents.[5] Genes that predispose to obesity in humans and animals have already been identified - the faulty gene -FTO, indicating the importance of genetic factor in the development of this disorder.[6]

Recent research has shown that the number as well as the size of adipocytes in obese people is more than people with normal body weight. Weight loss in an obese adult can reduce the size but not the number of adipocytes.[7] Hence these adults do retain the tendency to put on weight faster than normal individuals. Therefore, prevention as well as early intervention is crucial to fight obesity.

CRP is a trace protein normally present in the circulation of healthy subjects, with a medium concentration of 1 mg/ L increasing 1000 fold in response to infection, ischaemia, trauma, burns and inflammatory conditions and decrease just as rapidly with the resolution of the pathology.[8] Hence, it is an acute phase protein which gets elevated during episodes of acute-inflammation or infection.[9] It is synthesized by the liver in response to factor released by macrophages and fat cells.[10]

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The present torrent of studies regarding C – reactive protein in Cardio vascular disease and associated conditions is facilitated by the ready commercial availability of automated CRP assays and of CRP itself as a research reagent. In the mid 1990's, immunoassays for CRP, with greater sensitivity than those previously in routine use, revealed that increased C- reactive protein values, within the range previously considered normal, strongly predicts future coronary events.[12] The high sensitivity CRP is considered as an novel biomarker, since it measures even low levels of CRP in human serum or plasma.[13]

Obesity, mainly visceral, often associates with co-morbid conditions, like insulin resistance, glucose and lipid abnormalities, and hypertension, each one an independent cardiovascular risk factor per se.[14] Obesity is currently regarded as a proinflammatory state. Excess adiposity often correlates with abnormal production of several mediators which often associate with cardiovascular events.

Numerous studies also support an independent association between circulating levels of CRP, an inflammatory marker potently induced by IL-6 and TNF-α (in excess in the obesity state), and cardiovascular events. Many studies have suggested that higher BMI is associated with higher CRP concentrations indicating a state of low – grade inflammation. Elevated CRP levels were present in 27.6% women and 6.7 % men of US adult population in obese persons with BMI > 30.[16]

- The physiologic role of CRP is to bind to phosphocholine expressed on the surface of dead or dying cell (and some types of bacteria) in order to activate the complement system via the C1Q complex as an immunologic defense mechanism.[11]
- The adipokine imbalance characterizing obesity, including low levels of adiponectin, high levels of leptin, inflammatory mediators (IL-6 and TNF-α) and antifibrinolytic factors (PAI-1) may induce oxidative stress and endothelial dysfunction- initial steps of atherogenesis.[15]
- Classification of BMI:
- Underweight : 18.5
- Normal weight: 18.5-24.9
- Overweight : 25-29.9
- Obesity :
- Class 1 : 30-34.9
- Class 2 :35-39.9
- Class 3: ≥40

As many studies have been conducted regarding inflammatory markers related with Cardio vascular diseases, Diabetes mellitus, Hypertension, Metabolic syndrome, Cancer, Sleep – Breathing disorders, Chronic obstructive pulmonary diseases, Bronchial asthma, Postmenopausal women, PCOD's, Statin therapy etc., Only a few studies have been done based on the impact of hs CRP (High Sensitivity C – reactive protein) prevalence in obesity.

Due to the paucity of information for correlation between BMI and hs CRP in Indian settings, the present study was undertaken. Elevated hs-CRP levels in young obese individuals is an indication of an existing pro-inflammatory state in them, which might lead to complications in future. Hence this study may create awareness among young obese individuals regarding the risk factors of obesity and the importance of diet, life style modifications and physical activities and thereby help them to lead a healthy life. Thus the present study aimed to correlate the concentration of hs-CRP in obese individuals.

Objectives

1. To assess obesity by means of Quetelet index.
2. To assess the levels of Hs-CRP in relation to BMI.

MATERIALS AND METHODS

This is a cross sectional Study conducted at Medicine OPD, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet , Puducherry between the period October 2012 to August 2013. The study group included 8 males and 12 females in the age group of 17-30 years with BMI> 30. Persons with systemic diseases like Diabetes, Hypertension, Hyperlipidemia were excluded from the study. The Institutional Research Council and Ethical committee approval was obtained. The subjects included into the study were selected after obtaining informed consent.

HEIGHT: It was measured against a vertical board with an attached metric rule and a horizontal headboard was brought in contact with the upper most point on the head. It was recorded barefoot, with person standing on a flat surface and weight distributed evenly on both feet and heels together and the head positioned so that the line of vision is perpendicular to the body. The arms were hanging freely by the sides and the head, back, buttocks and heels were in contact with vertical board. The individual was asked to inhale deeply and maintained a full erect position. . The head was held erect with the external auditory apparatus and the lower border of the orbit in one horizontal plane. Top most point on the head with sufficient pressure to compress the hair was taken as height to the nearest of 0.1 cm.

WEIGHT: It was measured with subjects in light clothes and without shoes in erect posture using standard apparatus.weight was measured to the nearest 0.1 kg on a weighing machine (Electronic Weighing machine) .

BODY MASS INDEX

For the assessment of obesity, height and weight measurements were taken on each subject, and using Quetelet index, the value of BMI was calculated for each subject.

$BMI = \text{weight (kg)} / \text{height (m)}^2$

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HIGH SENSITIVITY C-REACTIVE PROTEIN

It was measured using Immunoturbidometer (Beacon): version 3.81 hsCRP kit: Code no -T05.

2 ml of blood was taken in a test tube and left undisturbed for half an hour for complete clot formation. The sample was then centrifuged at 3000 rpm to separate the serum from the clot. After centrifugation, the serum was stored at 20◦ C in Ependorf tubes till the analysis for hs-CRP was conducted. Serum hs-CRP levels were measured by turbidometry method. 17

Statistical Analysis

All the variables were expressed as mean ± SD. The data collected was entered in Microsoft Excel and analyzed using SPSS software package Version 19. Pearson correlation was used to analyse the relationship between hs CRP thresholds with BMI of obese individuals.

RESULTS

Total of 20 obese individuals were selected for the study of which 8 were males and remaining 12 were females categorized by calculating their BMI. The results were tabulated and analysed.

Among the 20 obese individuals (12 Females and 8 Males) whose BMI was categorized as Class I 30 to 34.9 Kg/ m2, Class II 35 to 39.9 Kg/ m2, Class III ≥ 40 Kg/ m2 respectively. Among them 60% of both males and females had BMI of Class I, 40% males and 33.3% females had BMI of Class II and 7% of females and none of the males had BMI of Class III which showed no significant association between BMI and gender distribution in obese individuals. [Table 1]

On the basis of gender, all the individuals included in this study were divided in two groups and were screened for the hs CRP levels. Total of 12 females and 8 males were screened and found that 80% females showed elevated hs CRP, as compared to 60% of males. The gender specificity was assessed for their association with hsCRP levels and no statistical significant association was reported (chi square 1.67 with a p value of > 0.5 NS). [Table 3]

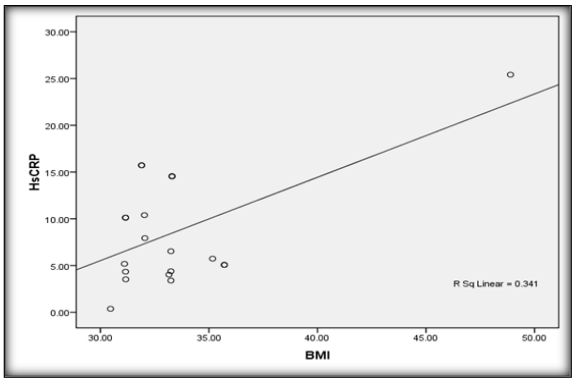

Figure 1: Scatter plot to show relation between BMI and hs CRP in study subjects

A total of 20 individuals were screened for the strength of association of obesity with high sensitivity CRP. Based on the BMI calculation they were categorized as obese subjects which showed that, there was a significant relationship between BMI and levels of hsCRP, Pearson correlation coefficient r = 0.59, P = 0.01. Obesity was associated with high values of hsCRP.

Table 1: Grading of Obesity in Subjects

Class	Number	Percent
1	16	80
2	3	15
3	1	5
Total	20	100

Table 2: BMI and Gender distribution in Study Subjects

BMI	Female n (%)	Male n (%)
30-34.9	9 (45)	7 (35)
35-39	2 (10)	1 (5)
≥ 40	1 (5)	0 (0)

Table 3: Association between hs CRP and gender in subjects

Reported hs CRP (mg/L)	Female n (%)	Male n (%)
≤ 3	0 (0)	1 (100)
≥ 3	12 (63.2)	7 (36.8)
Total	12 (60)	8 40)

DISCUSSION

Obesity is a long term disease having many serious consequences on the health of a person.[2] It is a state of excess adipose tissue mass and the most widely used method to calculate obesity is BMI.[1] Recently it has also been described as a pro inflammatory state which is involved in the pathophysiology of many diseases. The main aim of the present study was to explore the association between the body mass index and hsCRP level among the obese individuals.

Total of 20 obese individuals were selected for the study of which 8 were males and remaining 12 were females categorized by calculating their BMI. Among these individuals 43.3% were between the

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age 20-24 yrs, 23.3% were between 25-27 yrs of age and 33.3% were between the age 28-30 yrs.

Among the 20 obese (8 males and 12 females) individuals who were subjected to relative BMI by using Quetelet index, no statistical significant difference in BMI was observed among males and females. The similar observation was made by other studies determined by Deepa M,[19] and her colleagues and Desigamani Kanniyappan,[20] and his colleagues.

Obesity implies an excess of adipose tissue.[26] Is a complex interaction between genes and environment -long term energy imbalance - sedentary life style, excessive caloric consumption or both. Adipose tissue which is a passive storage depot for fat plays active role in metabolism.[27] Clinical measurements of adiposity plays the surrogate role for systemic inflammatory state of individuals.[28]

Obesity causes the structural and functional changes in various body sites i.e. skeletal muscle, liver, cardiovascular, integument, pulmonary, cerebral and coronary arteries. In recent reports obesity has linked with development of fatty liver diseases.[27]

The person with obesity is associated with elevated CRP which showed frequent episodes of infections. In obesity there is increased secretion of IL - 6 which activates the hepatic pathways to release the large amount of acute-phase proteins CRP in circulation.[28] The older experimental studies and cross-sectional studies have showed that CRP along with IL - 6 are contributing in the development of hyperglycemic, insulin resistance and Type 2 - DM.[29]

- This study shows elevated hs-CRP levels in relation to BMI3
- A higher BMI score was seen in female subjects
- Hs-CRP levels did not show variation in relation to gender
- A justifying finding was mentioned by Jeemon P26 et al who found a significant association between CRP and BMI comparing overweight and normal individuals (OR=3.90, CI=95%)
- Furthermore, Dogan Y et al studied CRP in relation to obesity and depression and concluded a positive correlation between CRP and BMI,[27]
- In contrast, Ishii S et al described an inverse proportion of CRP in relation to BMI in women
- From this it can be stated that hs-CRP correlates positively with BMI in obese subjects irrespective of gender

Limitations of the Study: Sample size should have been more in number for correlation of the study.

CONCLUSION

- This study suggests the occurrence of higher hs-CRP levels in relation to BMI in obese subjects.
- Elevated hs-crp levels in obese subjects indicates a proinflammatory state.
- This implies further risks for metabolic and cardiovascular manifestations in obese individuals.

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