Original Research Article

TO STUDY HIGH-SENSITIVITY CRP LEVELS IN OVERWEIGHT AND OBESE INDIVIDUALS

Abstract : . The present study examines whether overweight and obese are inter related with low-grade systemic inflammation as measured by serum hs-CRP concentration. The present observational, cross-sectional study is from the department of medicine, CSS Hospital, Subharti Medical College, Meerut, to evaluate the profile of patients who came for routine health check-ups from December 2020 to January 2022. The study comprised 150 patients divided into three groups normotensives, normoglycemic adults of the age group 20-70 years based on BMI as Normal BMI (18.5-22.9 kg/m^2), overweight (23-24.9 kg/m^2) and obese (BMI>25 kg/m^2), according to Asian standards by WHO. The mean age among the study subjects was 49.38±12.62 years. Out of 150 subjects, 83 (55.33%) were males and 67 (44.67%) were females. Normal, overweight, and obesity were found among 34%, 29.33%, and 36.67% of the subjects respectively. Normal and high hs-CRP was reported in 46% and 54% of the subjects respectively. The mean hs-CRP among the study subjects was 6.07±4.23. Mean FBS (mg/dL), WC (cm), TC (mg/dL), TGL (mg/dL), and HDL (mg/dL) among the study subjects was 102.94±13.03, 88.2±13.36, 161.84±52.56, 133.18±64.48 and 34.73±17.44 respectively. Mean hs-CRP was found to be highest in obese subjects (10.09±3.67) followed by overweight (6.74±2.48) and normal subjects (2.32±1.11). When hs-CRP was compared among normal vs overweight, normal vs obese, and overweight vs obese using a t-test, a significant difference was found. Pearson correlation analysis revealed a positive correlation between BMI, FBS (mg/dL), WC (cm), TC/HDL (mg/dL), TGL (mg/dL), and hs-CRP i.e. with an increase in these mentioned parameters, hs-CRP value also increases. **Conclusion**: Obesity is a state of chronic inflammation that has a strong link to hs-CRP levels.

Key words Hs-CRP, Obesity, Overweight, Chronic Inflammation

Introduction: The increasing number of o~~O~~verweight and o~~O~~besity individuals in India is a ~~primary~~ growing health concern ~~in India~~ due to an~~their~~ increasing prevalence in the younger and adult population[1,2]. Obesity makes th~~o~~ese people vulnerable to various metabolism-related diseases like diabetes mellitus, hypertension, ischaemic heart disease, cerebrovascular accidents, and cancers. Fat accumulation may be due to excess calorie intake, lack of exercise, and interactions of various socioeconomic, environmental, and genetic

factors[2,3]. The World Health Organization (WHO) estimates that 1 billion people are overweight worldwide, out of which 300 million are obese[4].

Adipose tissue produces numerous pro-inflammatory cytokines such as Interleukin-1 (IL-1), Tumour Necrosis Factor-α (TNF-α), and Interleukin-6 (IL-6), which are essential factors in the synthesis of hs-CRP in the liver. Elevated hs- CRP levels help predict future risk of diabetes mellitus, ischaemic heart diseases, and cerebrovascular accidents in healthy obese people[5].

Formerly, hs-CRP is considered a biomarker for inflammation. Still, it is a significant player in endothelial dysfunction and atherosclerosis.[6,7] hs-CRP is an essential precursor of metabolic syndrome (MetS) and type 2 diabetes and a strong predictor of early-stage cardiovascular disease (CVD) even when within the clinical normal reference range. Adipose tissue plays an important role in the induction of chronic low-grade inflammation via hs-CRP production in the liver by synthesizing cytokines, especially interleukin-6 (IL-6). Measures for overweight are among the strongest correlates of hs-CRP concentrations to such an extent that a close relationship between inflammation and overweight may help to explain the greater susceptibility to CVD among these individuals[8].

Positive correlations were present between IL-6, BMI, and percent fat mass (PFM). IL-6 also plays an anti-inflammatory role by reducing TNF-α and interferon-γ and stimulating IL-1RA. The proposed mechanism of this metabolic effect is the reduction of glucose transporter-4 and insulin receptor substrate-1 expression in response to IL-6 exposure[9]. The present study examines whether overweight and obese are inter related with low-grade systemic inflammation as measured by serum hs-CRP concentration.

Material and methods: The present observational, cross-sectional study is from the department of medicine, CSS Hospital, Subharti Medical College, Meerut, to evaluate the profile of patients who came for routine health check-ups from December 2020 to January 2022. The process and procedure of the study is explained to the participants and willing consent is obtained from them. Permission to carry out the study was acquired by the Institutional Ethical Committee of CSS Hospital, Subharti Medical College, Meerut.

Sample: The study comprised 150 patients divided into three groups normotensives, normoglycemic adults of the age group 20-70 years based on BMI as Normal BMI (18.5-22.9 kg/m^2), overweight (23-24.9 kg/m^2) and obese (BMI>25 kg/m^2), according to Asian standards by WHO[16].

Eligibility criteria:

a. ***Inclusion criteria –***

All subjects who had normal BMI (18.5-22.9 kg/m^2), overweight (23-24.9 kg/m^2), and obese (BMI>25 kg/m^2) were all used as a part of this study.

b. ***Exclusion criteria –***

The study excluded those patients with diabetes mellitus, malignancy, hypertension, Cardiovascular Disease (CVD), endocrinal and metabolic disorders, bronchial asthma, Chronic Obstructive Pulmonary Disease (COPD), autoimmune disorders, inflammatory diseases, and infectious diseases. The study also excluded smokers who were on steroids, statins, and anti-inflammatory drugs and who consumed alcohol.

Parameters used:

Height (m) was measured with the patient standing against a vertical surface, touching it with heels, buttocks, and back on a level smooth surface. The subject wearing everyday clothing, was made to stand in the center of an electronic weighing machine. Weight (kg) was recorded. BMI was calculated using the formula as Weight (kg)/ Height (m2). Waist Circumference (WC) was measured between the lower margin of the ribs and the upper border of the iliac crest after regular expiration. The hip circumference was measured accurately at the greater trochanters level, where the buttocks protrude the maximum. The limit for WC for men and women was 90 cm and 80 cm, respectively. WHR limit for men and women was 0.9 and 0.85, respectively[16].

Investigations

FBS, lipid parameters, and serum hs-HS-CRP levels were estimated in subjects, who were overnight fasting (approximately 12 hours) since the last dinner by drawing blood samples. The range of normal FBS and Impaired FBS was 70-100 mg/dL and 101-125 mg/dL, respectively. As per ATP III guidelines, the normal range of TC is 140-200 mg/dL, and TGL is 60-150 mg/dL. The average HDL Cholesterol and LDL Cholesterol levels are 40-60 mg/dL and 50-130 mg/dL, respectively. The normal level of hs-HS-CRP in adults is <5 mg/L.

Data Analysis: The data obtained were transferred to spreadsheets and analyzed using SPSS version 20.0. The results are presented as means ± standard deviation, percentages, and tables. Continuous variables were compared using the Student's *t-test*, while categorical parameters were analyzed with the Chi-square test or two-tailed Fischer's exact test as appropriate. A *P*-value of 0.05 or less will be considered statistically significant.

Results: The mean age among the study subjects was 49.38±12.62 years. Out of 150 subjects, 83 (55.33%) were males and 67 (44.67%) were females. Normal, overweight, and obesity were found among 34%, 29.33%, and 36.67% of the subjects respectively. Normal and high

Comment [John Scze1]: Please include results about your groups baselines. Were there significant differences in age or genders among the three groups. Gender and increasing age can effect CRP levels. From your data I cannot tell if age in the three groups was the same. Or that gender was similar in all groups. If they are comparable it will stengthen your argument even more. If they are not the same perhaps you could show the minimal effects compared to BMI.

hs-CRP was reported in 46% and 54% of the subjects respectively. The mean hs-CRP among the study subjects was 6.07±4.23 (table 1).

Table 1: Distribution of subjects according to gender, age, BMI, and hs-CRP values

Variables	**N=150**	**%**
Age in years, Mean±SD	49.38±12.62	
Gender		
Male	83	55.33
Female	67	44.67
BMI (kg/m^2)		
Normal	51	34.00
Overweight	44	29.33
Obese	55	36.67
hs-CRP		
Normal	69	46
High	81	54
hs-CRP, Mean±SD	6.07±4.23	

Mean FBS (mg/dL), WC (cm), TC (mg/dL), TGL (mg/dL), and HDL (mg/dL) among the study subjects was 102.94±13.03, 88.2±13.36, 161.84±52.56, 133.18±64.48 and 34.73±17.44 respectively (table 2).

Table 2: Baseline investigations among the study subjects

Variables	**Mean**	**SD**
FBS (mg/dL)	102.94	13.03
WC (cm)	88.2	13.36
TC (mg/dL)	161.84	52.56
TGL (mg/dL)	133.18	64.48
HDL (mg/dL)	34.73	17.44

Mean hs-CRP was found to be highest in obese subjects (10.09±3.67) followed by overweight (6.74±2.48) and normal subjects (2.32±1.11). When hs-CRP was compared among normal vs overweight, normal vs obese, and overweight vs obese using a t-test, a significant difference was found (table 3).

Table 3: Comparison of hs-CRP w.r.t. BMI

BMI (kg/m^2)	Mean hs-CRP	SD	p-value		
			Normal vs Overweight	Normal vs Obese	Overweight vs Obese
Normal	2.32	1.11			
Overweight	6.74	2.48			
Obese	10.09	3.67	0.007*	<0.01**	0.018*

*: statistically significant, **: highly significant

Pearson correlation analysis revealed a positive correlation between BMI, FBS (mg/dL), WC (cm), TC/HDL (mg/dL), TGL (mg/dL), and hs-CRP i.e. with an increase in these mentioned parameters, hs-CRP value also increases (table 4).

Table 4: Correlation between hs-CRP and other variables

Variables	r value	p-value
BMI	0.49	<0.01**
FBS (mg/dL)	0.42	0.002*
WC (cm)	0.45	0.001*
TC/HDL (mg/dL)	0.38	0.005*
TGL (mg/dL)	0.17	0.12

r: Pearson correlation, *: statistically significant, **: highly significant

Discussion: One of the factors which pose a considerable health risk, especially for cardiovascular diseases is obesity and overweight and elevated levels of CRP. CRP levels above 10 mg/l have been associated with an increased risk of myocardial infarction, ischemic stroke, and peripheral arterial disease. Raised CRP levels release IL6, which is observed in patients with angina. These levels are also expected to predict the incidence of cardiovascular disease in patients[7]. This study was conducted to evaluate whether overweight and obese are associated with low-grade systemic inflammation as measured by serum hs-CRP concentration.

In this study, the mean age among the study subjects was 49.38±12.62 years. Out of 150 subjects, 83 (55.33%) were males and 67 (44.67%) were females. Normal, overweight, and obesity were found among 34%, 29.33%, and 36.67% of the subjects respectively. Normal and high hs-CRP was reported in 46% and 54% of the subjects respectively. The

mean hs-CRP among the study subjects was 6.07±4.23. Similar baseline characteristics were reported by Kasukurti Lavanya et al[2] and Marjolein Visser et al[5] in their studies.

Mean hs-CRP was found to be highest in obese subjects (10.09±3.67) followed by overweight (6.74±2.48) and normal subjects (2.32±1.11). When hs-CRP was compared among normal vs overweight, normal vs obese, and overweight vs obese using a t-test, a significant difference was found in our study. Pearson correlation analysis revealed a positive correlation between BMI and hs-CRP in the present study. Kasukurti Lavanya et al[2] also found a substantial positive relationship between BMI and hs-CRP and the mean hs-CRP levels were higher in overweight and obese people when compared with people with normal BMI. Various authors such as Aronson D et al, Kao TW et al and Lin CC et al too reported similar findings in their studies.

In the present study, a positive correlation was found between WC (cm) and hs-CRP i.e. with an increase in WC, the hs-CRP value also increases. A similar positive relationship was established between central obesity (WC) and hs-CRP levels by Kao TW et al., and Laplace E et al., which demonstrated that abdominal adiposity is connected with higher C-reactive protein which was independent of BMI. In a study by Kasukurti Lavanya et al[2] too, waist circumference showed a significant positive correlation with hs-CRP.

WC is an indicator of central obesity. Indians have increased total body fat and increased accumulation of truncal and abdominal fat. This is why many Indian people even though they have normal body weight come under the category of the metabolically obese population. This typical “Asian Indian Phenotype”, with increased WC leads to hyperglycemia and premature coronary heart disease. Various studies in India revealed that 10% to 30% of adolescents are overweight. Decreased physical activity, consuming more junk foodstuffs, watching television programs, and sedentary lifestyles are common in younger people. These factors are responsible for the growing predominance of obesity and overweight. Hence, this signifies that abdomen adipose tissue is the chief source of cytokines like TNF- alpha, and IL-6, which are the main determining factor of hepatic synthesis of hs-CRP. These inflammatory mediators lead to endothelial dysfunction and atherosclerosis, which play a major part in the pathogenesis of ischaemic heart disease and other obesity-linked morbidity[2].

In our study; a positive correlation was found between TC/HDL (mg/dL), TGL (mg/dL), and hs-CRP i.e., with an increase in these mentioned parameters, the hs-CRP value also increases. However, no significant association was found between hs-CRP and TGL (mg/dL). In the Montenegro study among all lipid parameters, hs-CRP has a moderate

negative correlation with HDL whereas TGL, LDL, and TC were poorly correlated and were not statistically significant. Similar results were found in a study done by Vidyasagar S et al., where, TGL and HDL were not significant predictors of hs-CRP. In earlier published articles, affirmative correlations were established among levels of hs-CRP and blood glucose, triglycerides, and BMI, and negative associations were established with HDL cholesterol levels[2].

The limitation of the present study was a smaller sample size along with the cross-sectional design of the study. We used only one hs-CRP measurement that possibly not perfectly reveals long-term inflammatory status in the body.

Measurements of the serum concentration of IL-6 were not available in the present study. Although the results support the hypothesis that IL-6 produced by the adipocytes increases CRP concentration, a direct assessment of IL-6 concentration is needed in future studies to further test this hypothesis.

Conclusion: Obesity is a state of chronic inflammation that has a strong link to hs-CRP levels. Waist circumference, which correlates closely with hs-CRP levels, is a stronger predictor of central obesity in men. Obesity is becoming more prevalent among India's youth and adults as a result of a variety of circumstances, wreaking havoc on the country's socioeconomic and healthcare sectors. hs-CRP is a novel marker for future cardiovascular disease that can be used to identify risk and start treatment early.

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