

Association of C Reactive Protein and Obesity.

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ABSTRACT

Background: Adipose, a storage house of fat releases pro-inflammatory IL6 into circulation. One of the markers for inflammation is CRP which is raised due to any condition resulting in inflammation. Since inflammation can result in Cardiovascular disease, detection of CRP carries a great value in preventing morbidity and mortality. **Methods:** 569 patients above the age of 18 years, who visited the outpatient wards for examination of cardiovascular risk factors were included in the study. Detailed history, height, weight, Body mass index, were taken from all patients. Routine blood tests and CRP levels were done for all patients. CRP was done by chemi-luminescence method. **Results:** Clinically raised CRP levels were seen in 3 (1.3%) of the males and 33(9.5%) of the females, while elevated CRP was seen in 64(28.7%) males and in 129 (37.3%) females. 98 (43.9%) of males and 163 (47.1%) of the females were overweight with BMI 25-20 kg/m² and 11 (4.9%) males and 48 (13.9%) females had a BMI of over 30 kg/m². There was considerable increase in the CRP levels as BMI increased in both males and females but no males had clinically raised CRP levels when compared to the females. **Conclusion:** Our study has shown a significant association of raised CRP levels with overweight and obesity. As inflammation is one of the early markers for future CVD, it is imperative to take proper action to reduce morbidity and mortality.

Keywords: Cardio-vascular disease, C-reactive protein, Obesity.

INTRODUCTION

Obesity is one of the leading health concern as it is associated with Cardiovascular disease in adults and children.^[1] WHO estimates that more than 1.9 billion adults, 18 years and older, are overweight. Of these over 600 million are obese. In 2014, about 13% of the world's adult population (11% of men and 15% of women) were obese. While in children, 42 million under the age of 5 were either overweight or obese. Overweight is also associated with more number of deaths than underweight.^[2] Once considered a high-income country problem, overweight and obesity are now on the rise in low- and middle-income countries, particularly in urban settings.

Adipose, a storage house of fat plays an important role in metabolism.^[3,4] Pro-inflammatory cytokine interleukin 6 (IL6) is one of the compounds expressed in the human adipose tissues^[3,4] and released into circulation.^[5] About 25% of the total human IL6 is estimated to be produced by adipose tissue.^[4] IL6 are known to have inflammatory properties as a result, their liberation into the circulation incites low-grade systemic inflammation in persons with excess body fat.

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Recently, many studies have been conducted to link inflammation to the initiation and progression of

Cardiovascular disease and as a result, the detection of these inflammation, markers have become of utmost value to predict CVD.^[6,7]

CRP is seen in patients with inflammation but in low quantities in healthy patients without acute illness.^[5] In one particular study, it was observed that every 1-SD increase in CRP was shown to increase vascular risk by more than 60%.^[8] There have been a few studies in population of different sex, ethnicity and age where in as association between obesity and CRP have been established. We have in our study also tried to establish a link between obesity and elevated CRP levels in our population.

MATERIALS AND METHODS

This prospective study was conducted at Department of Medicine, MRIMS and MRMCW Hyderabad during August -2013 to July 2015. 569 patients above the age of 18 years, who visited the outpatient wards for examination for cardiovascular risk factors were included in the study. Patients with overt inflammatory diseases, pregnant women were excluded from the study. Detailed demographic details like age, sex, height and weight were taken for all the patients. As smoking is one of the risk factors of CVD, it was also taken into consideration. Amount of activity of all the patients was categorized as never, rarely, regular physical activity. Thorough physical examination was done including blood pressure was noted.

Blood tests for blood sugar levels, Triglycerides levels, cholesterol, complete blood picture, ESR were done. CRP levels were tested by chemi-luminiscence method. CRP levels were categorized as normal for levels ≤ 0.22 mg/dL, as elevated CRP for levels $>0.22-1.00$ mg/dL and as clinically raised levels in cases with >1.0 mg/dL.

BMI was used as an estimate for the obesity levels. It was calculated as $\text{Weight} / \text{Height}^2$. Based on the WHO categorization, the BMI was classified as normal <25 kg/m², overweight BMI 25.0–29.9 kg/m²; class I obese BMI 30.0–34.9 kg/m²; class II obese BMI 35.0–39.9 kg/m²; and class III obese BMI ≥ 40.0 kg/m².^[9]

RESULTS

Out of the 569 patients, 223(39.2%) were males and 346 (60.8%) were females. The mean age for the males was 56.8 ± 4.7 and for females it was 49.1 ± 3.8 . The mean weight of the males was 95.7 ± 3.6

and for females it was 68.7 ± 2.9 . Mean height of the males was 5ft 9 inches ± 3 in while for females it was 5 ft 1in ± 4 in [Table 1].

Only 3 (1.3%) of the males had clinically raised CRP levels while it was seen in 33(9.5%) of the females. Elevated CRP was seen in 64(28.7%) males and in 129 (37.3%) females [Figure 1]. All the other patients had CRP levels within limits.

Normal Body mass index was seen in majority of the patients, both males and females on the whole. But more number of females when compared to men had the tendency to be either overweight or obese. 98 (43.9%) of males and 163 (47.1%) of the females were overweight with BMI 25-20 kg/m². 11 (4.9%) males and 48 (13.9%) females had a BMI of over 30 kg/m² [Figure 2].

There was considerable increase in the CRP levels as BMI increased in both males and females but no males had clinically raised CRP levels when compared to the females [Table 2].

Table 1: Demographic details of the patients.

Parameter	Mean in males n= 223	Mean in females n= 346
Age	56.8 \pm 4.6	49.1 \pm 3.8
Weight	95.7 \pm 3.6	68.7 \pm 2.9
Height	5ft 9 inches \pm 3 in	5 ft 1in \pm 4in
Family history of Diabetes	87 (39%)	98 (28.3%)
Smoking status		
Never	89 (39.9%)	322 (93%)
Occasional	53 (23.8%)	9 (2.6%)
Regular	81 (36.3%)	15 (4.3%)
Alcoholism		
Never	89 (39.9%)	301(87%)
Occasionally	75 (33.6%)	36 (10.4%)
Regularly	59 (26.5%)	9 (2.6%)

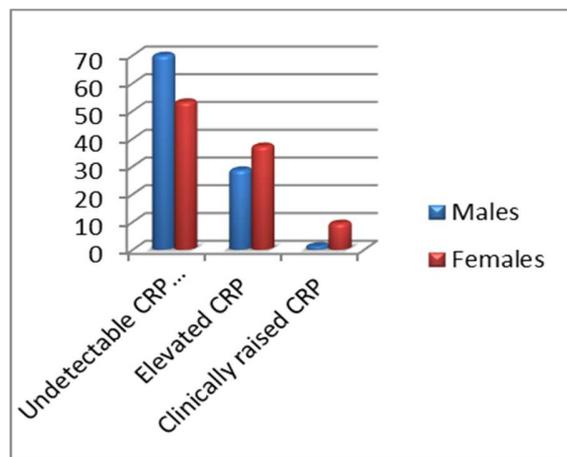


Figure 1: C Reactive Protein levels in males and females

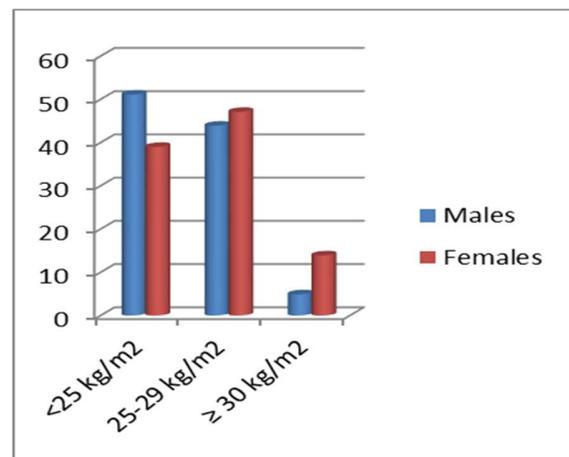


Figure 2: Body Mass Index in males and females

Table 2: Correlation of BMI with CRP levels in both males and females

Parameter	Males- BMI <25 kg/m ² n=114	Males - BMI 25-29kg/m ² n=98	Males - BMI ≥ 30kg/m ² n=11	Females-BMI <25 kg/m ² n=135	Females - BMI 25-29kg/m ² n=163	Females-BMI ≥ 30kg/m ² n=48
Elevated CRP	18(15.8%)	39(39.8%)	7(63.3%)	46 (34.1%)	65 (39.9%)	18 (37.5%)
Clinically raised CRP	1 (0.1%)	2 (2%)	0	3 (2.2%)	17 (10.4%)	13 (27.1%)

DISCUSSION

Overweight, obesity, and a large waist-to-hip ratio pose a considerable health risk, including cardiovascular health.^[10-12] Low-grade systemic inflammation with elevated CRP levels has been shown to increase the risk for cardiovascular disease. C-reactive protein concentrations well below the conventional clinical upper limit of normal of 1 mg/dL have been associated with a 2- to 3-fold increase in risk of myocardial infarction, ischemic stroke, and peripheral arterial disease in healthy men and women.^[13,14]

Raised levels of CRP in patients with angina is said to point to release of IL6 by activated macrophages.^[15,16] However, more recently it has been observed that elevated levels of CRP predicts the incidence of CVD in patients over years.^[17,18]

The mechanisms related to elevated CRP levels, CVD and obesity is poorly understood. The plausible cause could be that CRP is a very sensitive marker for systemic inflammation.^[19] They reflect the inflammation of coronary blood vessels which are related to atherogenic plaque related to Myocardial Ischemia or necrosis.^[20] It is also implicated that CRP levels reflect the amount of pro-inflammatory cytokines like TNF, IL1 and IL6 which are seen in atherosclerotic plaque formation.^[20,21] The secretion of IL6 occurs in many sites including in the adipose tissue which is probably the link between CRP, CVD and obesity.^[21]

Our study showed a prevalence of obesity and overweight opt be more in women than in men. Similar was the case with elevated and clinically raised CRP levels, where in we have shown a prevalence of elevated CRP levels in 28.7% males and 37.3% females. Clinically raised CRP levels were observed only in 1.3% of the males while 9.5% of the females had clinically raised CRP levels. The incidence of increased CRP levels was significant in patients who were either overweight or obese. This significance was acknowledged by Visser et al who observed that body fat was seen in females more than in males. Similarly CRP levels were raised more in females as well. This could be due to the fact that women tend to be more obese than men.^[22] This association of CRP levels with BMI was observed in many other researchers also like Saijo et al, who

found CRP was significantly associated with obesity in a study in Japan^[23] and Sutin et al.^[24]

In a study by Bastard et al, it was observed that weight loss induced a significant reduction in the adipose tissue IL6 levels in women trying to lose weight. They did observe a reduction in CRP levels though due to the small sample size, though this reduction could not be brought to significant levels.^[25]

In our study no association could be found between smoking and alcoholism on the CRP levels. This was in contrast to a study by Aronson et al who found statistical significance between CRP levels and all the components of metabolic syndrome including smoking.^[26]

CONCLUSION

Our study along with evidence from few other studies suggest a positive correlation between obesity and C reactive protein levels. These are even prominent in younger people. One of the risk for cardiovascular disease in overweight and obese persons is probably due to increased CRP levels in them. As a result it is imperative to take proper precautionary measures by overweight or obese patients with elevated CRP levels to prevent a myocardial infarction.

REFERENCES

- Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med.* 1999;340:448-54.
- WHO Fact sheet. Updated in Feb 2015: <http://www.who.int/mediacentre/factsheets/fs311/en/>
- Flier JS. The adipocyte storage depot or node on the energy information superhighway? *Cell.* 1995;80:15-8.
- Mohamed-Ali V, Pinkney JH, Coppack SW. Adipose tissue as an endocrine and paracrine organ. *Int J Obes Relat Metab Disord.* 1998;22:1145-58.
- Fried SK, Bunkin DA, Greenberg AS. Omental and subcutaneous adipose tissues of obese subjects release interleukin-6. *J Clin Endocrinol Metab.* 1998;83:847-50.
- Libby P, Ridker PM, Hansson GK. Inflammation in atherosclerosis: from pathophysiology to practice. *J Am Coll Cardiol* 2009;54:2129-38.
- Pearson TA, Mensah GA, Alexander RW. Markers of inflammation and cardiovascular disease. *Circulation* 2003;107:499-511.
- The Emerging Risk Factors Collaboration. C-reactive protein concentration and risk of coronary heart disease, stroke, and

- mortality: an individual participant meta-analysis. *Lancet* 2010;375:132–40.
9. World Health Organization Expert Committee. Physical status: the use and interpretation of anthropometry. WHO Technical Report Series No 854 1995 World Health Organization: Geneva
 10. Pi-Sunyer FX. Health implications of obesity. *Am J Clin Nutr*.1991;53:1595S-603S.
 11. Rexrode KM, Carey VJ, Hennekens CH. et al. Abdominal adiposity and coronary heart disease in women. *JAMA* 1998;280:1843-8.
 12. Folsom AR, Stevens J, Schreiner PJ, McGovern PG. Body mass index, waist/hip ratio, and coronary heart disease incidence in African-Americans and whites. *Am J Epidemiol*.1998;148:1187-94.
 13. Ridker PM, Buring JE, Shih J. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. *Circulation*.1998;98:731-3.
 14. Koenig W, Sund M, Frohlich M. C-reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men. *Circulation*.1999;99:237-42.
 15. Maseri A, Biasucci LM, Liuzzo G. Inflammation in ischemic heart disease. *BMJ*. 1996;312:1049–50.
 16. Haverkate F, Thompson SG, Pyke SDM, Gallimore JR, Pepys MB. Production of C-reactive protein and risk of coronary events in stable and unstable angina. *Lancet*. 1997;349:462–6.
 17. Mendall MA, Patel P, Ballam L, Strachan D, Northfield TC. C-reactive protein and its relation to cardiovascular risk factors: a population based cross sectional study. *BMJ*. 1996;312:1061–5.
 18. Ridker PM, Cushman M, Stampfer MJ, Tracey RP, Hennekens CH. Inflammation, aspirin and the risk of cardiovascular disease in apparently healthy men. *N Engl J Med*. 1997;336:973–9.
 19. Deodhar S. C-reactive protein: the best laboratory indicator available for monitoring disease activity. *Cleve Clin J Med*. 1989;56:126–30.
 20. Lagrand WK, Visser CA, Hermens WT. C-reactive protein as a cardiovascular risk factor. More than an epiphenomenon? *Circulation*. 1999;100:96–102
 21. Yudkin JS, Kumari M, Humphries SE. Inflammation, obesity, stress and coronary heart disease: is interleukin-6 the link? *Atherosclerosis*. 2000;148:209–14.
 22. Gallagher D, Visser M, Sepúlveda D. How useful is body mass index for comparison of body fatness across age, gender, and ethnic groups? *Am J Epidemiol*.1996;143:228-39.
 23. Saijo Y, Kiyota N, Kawasaki Y, Miyazaki Y, Kashimura J, Fukuda M, Kishi R; Relationship between C-reactive protein and visceral adipose tissue in healthy Japanese subjects. *Diabetes Obes metab* 2004 Jul;6(4):249-58.
 24. Angelina R Sutin, Yannick Stephan, Martina Luchetti, Antonio Teraciano; Perceived weight discrimination and C reactive Protein. *Obesity* 2004;22:1959-61.
 25. Bastard JP, Jardel C, Bruckert E. Elevated levels of interleukin 6 are reduced in serum and subcutaneous adipose tissue of obese women after weight loss. *J Clin Endocrinol Metab*. 2000;85:3338-42.
 26. D Aronson, P Bartha, O Zinder, A Kerner, W Markiewicz, O Avizohar et al. Obesity is the major determinant of elevated C-reactive protein in subjects with the metabolic syndrome. *Int J Obesity* 2004;28:674–9.

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