Journal of Medical Sciences

ISSN 1682-4474

science alert

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Research Paper

J. Med. Sci., 9 (1): 17-23
1st January, 2009

The Effect of Weight Reduction Diet on C-Reactive Protein Level in Obese-Adult Subjects

Adel A. Al-Hamdan, Rabba H. Al-Huthail, Mohamed A. Alsaif,
Abdulaziz M. Al-Othman, May N. Al-Muammer, Saada M. Al-Orf,
Abdallah A. Saeed and Badreldin A. Mohamed

To study the effect of weight-reduction diet (WRD) on serum high sensitivity C-reactive protein (hs-CRP) level in obese-adult subjects admitted to Riyadh Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia. Fifty three subjects with body mass index (BMI) $\geq$30 kg m^{-2} were included in the study. They were placed on energy-restricted diet for 12 weeks. Diet history and food-frequency questionnaire were filled before starting the WRD. Anthropometric measurements [weight, height, BMI and waist circumference (WC)] were taken and blood samples were collected to analyze hs-CRP, total cholesterol, triglyceride, high-density lipoprotein-cholesterol and low-density lipoprotein-cholesterol before and at the end of the WRD. There is a significant reduction in BMI and WC after applying the WRD program. In addition, hs-CRP level, triglyceride and total cholesterol were significantly reduced after applying the WRD. A significant positive correlation was noted between serum hs-CRP level and measures of adiposity, such as BMI and WC. hs-CRP level is influenced by WC and by BMI in obese-adult subjects and that the WRD decreases serum level of hs-CRP.

Key words: C-reactive protein, weight-reduction diet, obese, body mass index, waist circumference, lipid profile

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

For further information about this article or if you need reprints, please contact:

Dr. Adel A. Alhmdan,
Department of Community Health Sciences,
College of Applied Medical Sciences,
King Saud University,
P.O. Box 10219,
11433, Riyadh, Saudi Arabia

Tel: +96614693553
Fax: +96614693552

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Deparment of Community Health Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia

INTRODUCTION

C-reactive protein (CRP) is an acute-phase protein that is elevated several hundred-folds in response to infection and is considered to be a good marker of inflammation (Baltz *et al*., 1982; Pepys, 1996; Ridker, 2003). CRP is one of the markers predicting future cardiovascular disease. Several studies have reported that the risk for cardiovascular disease was positively associated with CRP levels (Tracy *et al*., 1997a, b; Danesh *et al*., 1998; Koenig *et al*., 1999; Rohde *et al*., 1999; Ridker, 2000; Ridker *et al*., 2000a). Ridker *et al*. (2002) have found that CRP is a better marker than low density lipoprotein-cholesterol (LDL-C) in predicting future coronary events and those subjects with high CRP and low LDL-C were at higher coronary risk than those with high LDL-C but low CRP. CRP is also positively associated with an increased risk of myocardial infarction and stroke (Ridker *et al*., 1997; Fored and Giles, 2000; Mendall *et al*., 2000; Ridker *et al*., 2000b; Rost *et al*., 2001).

Obesity and accumulation of fat surrounding the abdominal visceral organs is associated with a variety of serious health conditions (Kissebah and Krakower, 1994). A disturbance in lipoprotein metabolism, which is a risk factor for atherosclerosis, has been reported in subjects with an excessive deposition of adipose tissue at the abdominal level (Kissebah *et al*., 1989; Després *et al*., 1990).

Proinflammatory cytokines, including interleukine-6 (IL-6), is expressed in human adipose tissues and then released into the circulation (Purohit *et al*., 1995; Mohamed-Ali *et al*., 1997; Fried *et al*., 1998). Adipose tissue is estimated to produce about 25% of systemic IL-6 *in vivo* (Mohamed-Ali *et al*., 1997). Adipose tissue-derived cytokines, particularly IL-6, is involved in the elevation of CRP in obesity (Bastard *et al*., 1999). The inflammatory properties of the proinflammatory cytokines, including the stimulation of acute-phase protein production in the liver, mild elevation of serum inflammatory cytokines and CRP may explain the increased cardio and cerebrovascular morbidity and mortality, particularly in morbidly obese patients (Flegal *et al*., 2002). The relationship between nutritional status and CRP level is ill defined. To the best of our knowledge no study has been conducted in KSA to assess the affect of dietary intervention on C-reactive protein level. Nationwide studies in the Kingdom of Saudi Arabia (KSA), reported an overall prevalence of 36.9% for overweight and 35.6% for obesity among adult Saudi males (Al-Nozha *et al*., 2004, 2005).

The main objective of the study is to examine the effect of weight-reduction diet (WRD) on high sensitivity CRP (hs-CRP) level in obese-adult subjects at Riyadh Armed Forces Hospital (RAFH), KSA.

MATERIALS AND METHODS

Setting: The study was conducted at RAFH, Riyadh, KSA. RAFH provides medical services for the military personnel and their dependents in KSA.

Subjects: Fifty three obese adults (age 18-60) with a body mass index (BMI) $\geq$30 kg m^{-2} referred from primary health care clinics to the nutrition clinic who satisfied inclusion criteria were included in the study. The exclusion criteria were: the presence of diabetes mellitus, cardiovascular disease, hypertension, inflammatory and autoimmune diseases and the use of anti-inflammatory or lipid-lowering drugs.

The study was approved by the local ethics committee. All participants gave their informed consent, after a full explanation of the nature of the study and the data collected will be used only for the stated research objectives.

Data collection: Data collection was carried out over a period of 5 months (from the 8th of February 2005 to the 9th of July 2005). The subjects were instructed to follow a WRD for a period of 12 weeks and written material diet sheet was provided. As the study duration is limited, the total energy content of the WRD was restricted to 1200 kcal, in which macronutrients constitute [50% carbohydrate (40% complex carbohydrate), 20% protein (14% high biological value protein) and 30% fat (10% saturated, 13% unsaturated and 7% monounsaturated fat)] of total kcal. Subjects were asked to visit the nutrition clinic every 3 weeks for dietary counseling and weight check.

Before starting the WRD program, demographic data and diet history were obtained. In addition, dietary habits were evaluated and the quantity of carbohydrate, protein and fat eaten by obese subjects at baseline, before entering the diet program, was estimated using the semi quantitative food frequency questionnaire.

Anthropometric variables: Anthropometric measurements and blood samples were taken before and at the end of the diet program. For anthropometric measurements, weight, height, BMI and waist circumference (WC) were measured. Subjects were weighed to the nearest 0.1 kg without shoes, with body weight evenly distributed between both feet using an electronic scale. Height was measured by a portable stadiometer and to the nearest 0.1 cm. BMI was calculated by dividing the weight in kilograms by the square of the stature in meters (kg m^{-2}). WC is used to assess abdominal fat distribution. WC was measured as the smallest dimension between the lower rib margin and the iliac crest and it was measured to the nearest 0.1 cm.

Sample collection and preparation: Venous blood samples obtained by venesection of the antecubital fossa vein with a 21 gauge venflon needle were taken from subjects after fasting for 9 h. The serum was separated and stored at -70°C until analysis. Serum lipid concentrations [total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and triglyceride (TAG)] were measured by enzymatic colorimetric methods using commercial reagent sets (Roche Diagnostics). LDL-C was calculated using the friedewald formula (Friedewald *et al*., 1972): LDL-C = TC-HDL-C-TAG/5. Serum hs-CRP was measured using a high-sensitivity monoclonal antibody to CRP coated on polyesterene beads (Siemens Health Care Diagnostics, Riyadh, KSA). Serum hs-CRP >3.00 mg L^{-1} was considered as a high risk value for cardiovascular disease (Pearson *et al*., 2003).

hs-CRP was measured instead of the traditional CRP method. Both CRP and hs-CRP measure the same molecule in the blood. The hs-CRP test measures very small amounts of CRP in the blood and is ordered most frequently for seemingly healthy people to assess their potential risk for heart problems. It measures CRP in the range from 0.5 to 10 mg L^{-1}. The CRP test is ordered for patients at risk for infections or chronic inflammatory diseases and it measures CRP in the range from 10 to 1000 mg L^{-1} (Leduc *et al*., 1998; Rifai *et al*., 1999), thus, hs-CRP was measured instead of the traditional CRP method.

Statistical analysis: Data were expressed as mean (M)±standard deviation (SD). In addition to the descriptive statistics, mean values at baseline and at the end of the diet program were compared using paired t-test. Correlation analysis were performed by calculating pearson correlation coefficient (r). A p-value of <0.05 was considered significant in all statistical tests. All statistical tests were computed using SPSS version 14 for Windows.

RESULTS

The data obtained for males, females and age were combined, since present results showed no gender difference in hs-CRP concentration (t-test; p = 0.334) and no age differences (ANOVA, p = 0.677). The general characteristics of the study sample are shown in Table 1. The majority of the subjects were females (81.1%), mostly married (67.9%) and about 74% of the subjects had educational level below the university level. Most subjects (81.2%) had monthly income of ≥3000 Saudi Riyal (1 US Dollar = 3.75 Saudi Riyal) and about 55% were unemployed. Using the semi-quantitative food frequency questionnaire, the results showed that the mean energy intake of the subjects, before entering the WRD program, was 3006 kcal day^{-1} and the percentage of energy intake from fat was high (Table 2).

Table 3 shows the anthropometric measurements and serum hs-CRP level of the subjects before and after the diet program. There were significant reductions in BMI, WC and hs-CRP level after applying the diet program when compared to the baseline. Table 4 displays the classification of subjects according to their hs-CRP level, at baseline and post treatment. The result demonstrated

Table 1: General characteristics of subjects

Variables	No.	Percentage	Mean±SD
Gender			
Female	43	81.1	
Male	10	18.9	
Material status			
Single	17	22.1	
Married	36	67.9	
Education level			
Illiterate	6	11.3	
Elementary	7	13.2	
Intermediate	10	18.8	
Secondary	16	30.2	
University and above	14	26.5	
Occupation			
Employed	24	45.3	
Unemployed	29	54.7	
Income/month (Saudi Riyal)			
<3000	10	18.8	
3000-5000	8	15.1	
>5000-8000	18	34.0	
≥8000	17	32.1	
Weight (kg)			92.2±2.48
Height (cm)			160.0±1.03

Table 2: Daily average energy intake and macronutrient intake of the subjects at base line

Energy and macronutrient intake	Value
Total energy intake	3006±249 (kcal)
Energy intake from carbohydrate	51%
Energy intake from protein	10%
Energy intake from fat	39%

Total energy intake is presented as Mean±SD. Energy intake from macronutrient is presented in percentage (%) of total energy intake

Table 3: Anthropometric measurements and serum hs-CRP level of the subjects before and after applying the diet program

Anthropometric measurements and hs-CRP	Pre (baseline)	Post (treatment)	p-value
BMI (kg m^{-2})	35.60±0.86	33.10±0.510	0 000
WC (cm)	101.90±1.690	93.00±1.730	0.000
hs-CRP (mg L^{-1})	6.01±0.72	4.70±0.55	0.007

BMI: Body mass index; WC: Waist circumference; hs-CRP: C-reactive protein

Table 4: Classification of subjects according to their C-reactive protein level before and after applying the diet program

	Pre (baseline)		Post (treatment)	
hs-CRP (mg L^{-1})	No.	%	No.	%
Acceptable level (<3 mg L^{-1})	21	39.6	27	51
High level (>3 mg L^{-1})	32	60.4	26	49

hs-CRP: C-reactive protein R; CHD: Coronary heart disease

Table 5: Comparison between lipid profile of the subjects before and after applying the diet program

Lipid profile (mg dL^{-1})	Pre (baseline)	Post (treatment)	p-value
TC	181.30±4.56	172.5±3.89	0.039
LDL-C	106.60±3.90	102.1±3.69	0.229
HDL-C	54.20±1.9	52.9±1.98	0.142
TG	100.10±7.38	90.8±6.24	0.028

TC: Total cholesterol; LDL-C: Low density lipoprotein-cholesterol; HDL-C: High density lipoprotein-cholesterol; TG: Triglyceride

Table 6: Correlation between various parameters and hs-CRP before and after implementing the diet program

	Pre (baseline)		Post (diet program)	
Variables	r	p-value	r	p-value
Age	0.024	0.862	0.028	0.878
BMI	0.339	0.024	0.322	0.024
WC	0.305	0.033	0.312	0.042
TC	0.029	0.837	0.157	0.261
LDL-C	0.025	0.862	0.184	0.186
HDL-C	-0.142	0.310	-0.031	0.825
TG	0.150	0.284	0.005	0.973

BMI: Body mass index; WC: Waist Circumference; hs-CRP: C-reactive protein; TC: Total cholesterol; LDL-C: Low density Lipoprotein-cholesterol; HDL-C: High density Lipoprotein-cholesterol; TG: Triglyceride; r: Correlation coefficient

that more than half of the subjects had a high level of hs-CRP at base line, before starting the diet program. The percentage was reduced to 49% after the diet program was implemented. Table 5 presents the lipid profile of the subjects before and after implementing the diet program. There was significant decrease in the serum TC and TG concentrations, after applying the program. A reduction in the serum LDL-C and HDL-C concentrations occurred, after applying the diet program, but it was not significant. The main meal for two thirds of the subjects (66%) was lunch and about half of the subjects skip breakfast. Nearly half of subjects consume whole fat dairy products and 43.4% of the subjects used to consume one snack daily (data not shown).

Table 6 outlines the correlation between hs-CRP and different parameters before and after applying the diet program. A significant positive correlation was found between hs-CRP and BMI or WC, either before or after implementing the diet program.

DISCUSSION

Several prospective epidemiologic studies have demonstrated a positive association between CRP levels and the risks of future cardio-vascular disease (Liuzzo *et al*., 1994; Thompson *et al*., 1995; Kuller *et al*., 1996; Haverkate *et al*., 1997; Tracy *et al*., 1997a, b; Koenig *et al*., 1999; Ridker *et al*., 2002). It has been suggested that blood CRP levels reflect the amount and activity of pro-inflammatory cytokines. There was a significant reduction in IL-6, by following a low-calorie diet and a trend toward reduced hs-CRP was noted, but the reduction was not statistically significant, after weight loss in obese women (Bastard *et al*., 2000). The insignificant reduction in CRP levels, after weight loss, could be attributed to the short duration of the weight loss program (3 weeks) and smaller number of subjects (n = 14) enrolled in their study. In the present study, hs-CRP decreased significantly, after the WRD program was applied.

WC and waist-to-hip ratio are the two most commonly used anthropometric measurements for the prediction of visceral adipose tissue. WC correlates with visceral adipose tissue more than the waist-to-hip ratio index (Simone *et al*., 1996). Abnormal WC is associated with disturbances in lipoprotein-lipid profile and even at the same level of overweight, an individual with a greater amount of visceral fat is more likely to have many of the metabolic complications, including cardiovascular disease (Montague *et al*., 1997; Stevens, 1995; Conway *et al*., 1995; Larsson, 1988). In a population-based study of 186 healthy women aged 43 to 55 years, Hak ***et al.*** (1999) reported that CRP was strongly related to WC, even after adjustment for BMI. They suggested that abdominal fat deposition could be an important determinant of inflammatory metabolic state. A significant positive correlation was also noted between CRP levels and BMI (Mendall *et al*., 1997; Tracy *et al*., 1997a, b). Approximately 25% of circulating IL-6 is estimated to be released by human subcutaneous adipose tissue in vivo and IL-6 stimulates the production of CRP in the liver (Nesbitt *et al*., 2004; Al-Qahtani *et al*., 2005). This might explain the reduction in hs-CRP levels and the positive association that was found between hs-CRP level and BMI or WC, either before or after applying the diet program (Table 6).

Elevated CRP levels have been reported among subjects with high TG and low HDL-C (Mendall *et al*., 1996; Tracy *et al*., 1997a, b; Hak *et al*., 1999; Yudkin *et al*., 1999). The relationship between IL-6, CRP and lipid profile could explain the benefit of reducing weight and avoiding central obesity in reducing the risk of CHD. In the present study, hs-CRP level (Table 3), TC and TG (Table 5), were reduced after the WRD program was implemented, but no significant correlation was observed between hs-CRP and lipid profile (Table 6). Present finding is in agreement with

Isabell *et al*. (2001) who found no significant correlation between plasma CRP levels and TC, TG, LDL-C, or HDL-C concentration in men aged 22 to 63 years.

To conclude, the results indicate that hs-CRP level is affected by BMI and WC in adults and that WRD decreases hs-CRP level in obese-adult subjects. Applying a WRD program to healthy-obese subjects may help in reducing the risk of CHD by reducing the amount of adipose tissues and thus, may down regulate CRP production. Pro-inflammatory cytokines were not measured in the present study, thus, direct assessment of these cytokines is needed in future relevant studies.

ACKNOWLEDGMENTS

Thanks to Mr. Khalid Al Helal, head of the dietetic department at the RAFH, for his support in conducting the study. The authors are also grateful to Dr. Samia sobki and her laboratory team at RAFH for their valuable assistant in the laboratory.

REFERENCES

Al-Nozha, M.M., M.R. Arafah, Y.Y. Al-Mazrou, M.A. Al-Maatouq and M.Z. Khan *et al*., 2004. Coronary artery disease in Saudi Arabia. Saudi. Med. J., 25: 1165-1171.

Al-Nozha, M.M., Y.Y. Al-Mazrou, M.A. Al-Maatouq, M.R. Arafah and M.Z. Khalil *et al*., 2005. Obesity in Saudi Arabia. Saudi Med. J., 26: 824-829.

Al-Qahtani, D., M. Imtiaz and M. Shareef, 2005. Obesity and cardiovascular risk factors in Saudi adult soldiers. Saudi Med. J., 26: 1260-1268.

Baltz, M.L., F.C. De-Beer, A. Feinstein, E.A. Munn and C.P. Milstein *et al*., 1982. Phylogenetic aspects of C-reactive protein and related proteins. Ann. N. Y. Acad. Sci., 389: 49-75.

Bastard, J.P., C. Jardel, J. Delattre, B. Hainque, E. Bruckert and F. Oterline, 1999. Evidence for a link between adipose tissue interleukin-6 content and serum C-reactive protein concentration in obese subjects. Circulation, 99: 2221-2222.

Bastard, J.P., C. Jardel, E. Bruckert, P. Blondy and J. Capeau *et al*., 2000. Elevated levels of interleukin 6 are reduced in serum and subcutaneous adipose tissue of obese women after weight loss. J. Clin. Endocr. Metab., 85: 3338-3342.

Conway, J.M., S.Z. Yanovski, N.A. Avila and V.S. Hubbard, 1995. Visceral adipose tissue difference in black and white women. Am. J. Clin. Nutr., 61: 765-771.

Danesh, J., R. Collins, P. Appleby and R. Peto, 1998. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: Meta-analysis of prospective studies. J. Am. Med. Assoc., 279: 1477-1482.

Després, J.P., S. Moorjani, P.J. Lupien, A. Tremblay, A. Nadeau and C. Bouchard, 1990. Regional distribution of body fat. Plasma lipoproteins and cardiovascular disease. Arteriosclerosis, 10: 497-511.

Flegal, K.M., M.D. Carroll, G.L. Ogden and C.L. Johnson, 2002. Prevalence and trends in obesity among US adults 1999-2000. J. Am. Med. Assco., 288: 1723-1727.

Fored, E.S. and W.H. Giles, 2000. Serum C-reactive protein and self-reported stroke: Finding from the third national health and nutrition examination survey. Arterioscler. Thromb. Vasc. Biol., 20: 1052-1056.

Fried, S.K., D.A. Bunkin and A.S. Greenberg, 1998. Omental and subcutaneous adipose tissues of obese subjects release interleukin-6. J. Clin. Endocr. Metab., 83: 847-850.

Friedewald, W.T., R.I. Levy and D.S. Fredrickson, 1972. Estimation of plasma low-density lipoprotein cholesterol concentration without use of the preparative ultracentrifuge. Clin. Chem., 18: 499-512.

Hak, A.E., C.D. Stehouwer, M.L. Bots, K.H. Polderman and C.G. Schalkwijk *et al*., 1999. Associations of C-reactive protein with measures of obesity, insulin resistance and subclinical atherosclerosis in healthy, middle-aged women. Arterioscler. Thromb. Vasc. Biol., 19: 1986-1991.

Haverkate, F., S.G. Thompson, S.D. Pyke, J.R. Gallimore and M.B. Pepys, 1997. Production of C-reactive protein and risk of coronary events in stable and unstable angina: European concerted action on thrombosis and disabilities angina pectoris study group. Lancet, 349: 462-466.

Isabelle, L., P. Agnès, P. Denis, A. Natalie and B. Peter *et al*., 2001. Elevated C-reactive protein: Another component of the atherothrombotic profile of abdominal obesity. Arterioscl. Throm. Vasc., 21: 961-967.

Kissebah, A.H., A.N. Peiris and D.J. Evans, 1989. Biology of regional body fat distribution: Relationship to non-insulin-dependent diabetes mellitus. Diabetes. Metab. Rev., 5: 83-109.

Kissebah, A.H. and G.R. Krakower, 1994. Regional adiopsly and morbidty. Physiol. Rev., 74: 761-811.

Koenig, W., M. Sund, M. Frohlich, H.G. Fischer and H. Lowel *et al*., 1999. C-Reactive protein a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men: Results from the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) augsburg cohort study, 1984 to 1992. Circulation, 99: 237-242.

Kuller, L.H., R.P. Tracy, J. Shaten and E.N. Meilahn, 1996. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study: Multiple risk factor intervention trial. Am. J. Epidemiol., 144: 537-547.

Larsson, B., 1988. Fat Distribution and Risk for Death Myocardial Infarction and Stroke. In: Fat Distribution during Growth and Later Health Outcomes, Bouchard, C. and F.E. Johnston (Eds.). Alan R. Liss, New York, pp: 193-201.

Leduc, T.B., D.L. Weiner, J.D. Sipe, S.E. Poulin, M.F. Collins and N. Rifai, 1998. Analytical evaluation of particle enhanced immune phelomtric assays for C-reative protein serum amyloid A and mannose-binding protein in human serum. Ann. Clin. Biochem., 35: 745-753.

Liuzzo, G., L.M. Biasucci, J.R. Gallimore, R.L. Grillo and A.G. Rebuzzi *et al*., 1994. The prognostic value of C-reactive protein and serum amyloid a protein in severe unstable angina. N. Engl. J. Med., 331: 417-424.

Mendall, M.A., P. Patel, L. Ballam, D. Strachan and T.C. Northfield, 1996. C-reactive protein and its relation to cardiovascular risk factors: A population based cross sectional study. Br. Med. J., 312: 1061-1065.

Mendall, M.A., P. Patel, M. Asante, L. Ballam and J. Morris *et al*., 1997. Relation of serum cytokine concentrations to cardiovascular risk factors and coronary heart disease. Heart, 78: 273-277.

Mendall, M.A., D.P. Strachan, B.K. Butland, L. Ballam and J. Morris *et al*., 2000. C-reactive protein relation to total mortality, cardiovascular mortality and cardiovascular risk factors in men. Eur. Heart. J., 21: 1584-1590.

Mohammed-Ali, V., S. Goodrik, A. Rawesh, D.R. Katz and J.M. Miles *et al*., 1997. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, *in vivo*. J. Clin. Endocr. Metab., 82: 4196-4200.

Montague, C.T., J.B. Prins, L. Sanders, J.E. Digby and S. O'Rahilly, 1997. Depot-and sex-specific differences in human leptin MRNA expression. Implications for the control of regional fat distribution. Diabetes, 46: 342-347.

Nesbitt, S.D., M.O. Ashaye, N. Stettler, J.M. Sorot and M.I. Goran *et al*., 2004. Overweight as a risk factor in children a focus on ethnicity. Ethn. Dis., 14: 94-110.

Pearson, T.A., G.A. Mensah, R.W. Alexander, J.L. Anderson and R.O. Cannon *et al*., 2003. Markers of inflammation and cardiovascular disease: Application to clinical and public health practice: A statement for healthcare professionals from the centers for disease control and prevention and the American heart association. Circulation, 107: 499-511.

Pepys, M.B., 1996. The Acute Phase Response and C-Reactive Protein. In: Oxford Textbook of Medicine, Weatheral, D.J., J.G.C. Lendingham, D.A. Warrell (Eds.). Oxford University Press, New York, pp: 1527-1533.

Purohit, A., M.W. Ghilchik, L. Duncan, D.Y. Wang, A. Singh, M.M. Walker and M.J. Reed, 1995. Aromatase activity and malignant breast tissues. J. Clin. Endocr. Metab., 80: 3052-3058.

Ridker, P.M., M. Cushman, M.J. Stampfer, R.P. Tracy and C.H. Hennekens, 1997. Inflammation, aspirin and risk of cardiovascular disease in apparently healthy men. N. Engl. J. Med., 336: 978-979.

Ridker, P.M., 2000. Novel risk factors and markers for coronary disease. Adv. Int. Med., 45: 391-418.

Ridker, P.M., C.H. Hennekens, J.G. Buring and N. Rifai, 2000a. C-reactive protein and other marker of inflammation in the prediction of cardiovascular disease in women. N. Engl. J. Med., 342: 836-843.

Ridker, P.M., N. Rifai, M.J. Stampfer and C.H. Hennekens, 2000b. Plasma concentration of interluken-6 and the risk of future myocardial infarction among apparently healthymen. Circulation, 10: 1767-1772.

Ridker, P.M., N. Rifai, L. Rose and E. Julis, 2002. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N. Engl. J. Med., 347: 1557-1565.

Ridker, P.M., 2003. C-Reactive a simple test to help predict risk of heart attack and stroke. Circulation, 108: 81-85.

Rifai, N., R.D. Tracy and P.M. Ridker, 1999. Clinical efficacy of an automated high-sensitivity C-reative assay. Clin. Chem., 45: 2136-2141.

Rohde, L.E., C.H. Hennekens and P.M. Ridke, 1999. Survey of C-reactive protein and cardiovascular risk factor in apparently healthy man. Am. J. Cardiol., 84: 1018-1022.

Rost, N.S., P.A. Wolf, C.S. Kase, M. Kelly-Hayes and H. Silbershatz *et al*., 2001. Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack, the Framingham Study. Stroke, 32: 2575-2579.

Simone, L., P.C. Denis, T. Angelo and D. Jean-Pierre, 1996. A single threshold value of waist girth identifies normal-weight and overweight subjects with excess visceral adipose tissue. Am. J. Clin. Nutr., 64: 685-693.

Stevens, J., 1995. Obesity fat patterning and cardiovascular risk. Adv. Exp. Med. Biol., 369: 21-27.

Thompson, S.G., J. Kienast, S.D. Pyke, F. Haverkate and J.C. Van-de-Loo, 1995. Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris: European concerted action on thrombosis and disabilities angina pectoris study group. N. Engl. J. Med., 332: 635-641.

Tracy, R.P., B.M. Psaty, E. Macy, E.G. Bovill and M. Cushman, 1997a. Lifetime smoking exposure affects the association of C-reactive protein with cardiovascular disease risk factors and subclinical disease in healthy elderly subjects. Arterioscl. Throm. Vasc., 17: 2167-2176.

Tracy, R.P., R.N. Lemaitre, B.M. Psaty, D.G. Ives and R.W. Evans *et al*., 1997b. Relationship of C-reactive protein to risk of cardiovascular disease in the elderly: Result from the cardiovascular health study and rural health promotion project. Arterioscl. Throm. Vasc., 17: 1121-1127.

Yudkin, J.S., C.D. Stehouwer, J.J. Emeis and S.W. Coppack, 1999. C-reactive protein in healthy subjects: Associations with obesity, insulin resistance and endothelial dysfunction: A potential role for cytokines originating from adipose tissue? Arterioscl. Throm. Vasc., 19: 972-978.