Original Article#

Association of Leukocyte Count and hsCRP with Metabolic Abnormalities in Subjects with Normal Glucose Tolerance (CURES – 64)

K Gokulakrishnan, R Deepa, R Sampathkumar, M Balasubramanyam, V Mohan

Abstract

Objective : The aim of the present study was to assess the association of leukocyte count and high sensitivity C-Reactive protein (hsCRP) with metabolic abnormalities in subjects with normal glucose tolerance.

Methods : Subjects with Normal Glucose Tolerance (NGT) (n = 865) were recruited from the Chennai Urban Rural Epidemiology Study [CURES]. Standard methods were used for assessing hsCRP [Nephelometry, in a subset] and leukocytes [Flowcytometry, Sysmex SF-3000]. Insulin resistance was calculated using the Homeostasis Assessment model (HOMA-IR).

Results : Body mass index, waist circumference, systolic and diastolic blood pressure, fasting plasma glucose, HbA_1c, serum cholesterol, LDL cholesterol, HOMA IR and hsCRP increased significantly with increasing tertiles of leukocyte count [p for trend < 0.001]. Both leukocyte count and hsCRP showed a positive correlation with cardiovascular risk factors. Leukocyte count showed a positive correlation with hsCRP [p=0.008]. Both mean leukocyte count [p<0.001] and hsCRP [p=0.04] were higher in subjects with Metabolic Syndrome (MS), which increased with increase in number of metabolic abnormalities [p for trend <0.001]. Regression models showed leukocyte count [p<0.001] and hsCRP [p=0.03] to be associated with MS, even after adjusting for age and gender.

Conclusion : A significant association exists between systemic inflammation [leukocyte count and hsCRP] and MS/ cardiovascular risk factors in Asian Indians even among non-diabetic subjects. ©

Introduction

Increased predisposition to diabetes and coronary artery disease (CAD) among Asian Indians has long been recognized.[1-2] Insulin resistance is considered to be one of the underlying causes for both glucose intolerance and CAD.[3] Insulin resistance clusters with many other metabolic abnormalities, which are collectively known as metabolic syndrome [MS].[3] Recent studies have reported that inflammatory markers like leukocyte count[4] and high sensitivity C-reactive protein [hsCRP][5] are associated with cardiovascular risk factors and MS. Indeed, elevated leukocyte count has been reported to be a predictor of cardiovascular mortality independent of traditional cardiovascular risk factors.[6] Leukocytes contribute to blood viscosity, release products that induce plaque rupture and thrombus formation,[7] and play a role in endothelial dysfunction.[8] Recent studies have also shown leukocyte count to be positively associated with carotid atherosclerosis,[9] a preclinical atherosclerotic marker and various components of MS and negatively associated with measures of insulin sensitivity. Prospective studies have indicated leukocyte count to be a predictor of type 2 diabetes.[10]

High hsCRP levels have been associated with a higher risk of cardiovascular morbidity and mortality in healthy subjects.[5,11] Measurement of hsCRP has been shown to add to the predictive ability of the Framingham risk score.[12] Several studies have shown an association between hsCRP and the various components of metabolic syndrome, especially diabetes, obesity and CAD among Europeans.[13-15]

A recent analysis of global and regional mortality indicated that Asian Indians had the highest mortality rates due to ischemic heart disease.[2,16] We earlier reported that hsCRP is associated with diabetes and CAD in Asian Indians.[17] However, there are hardly any studies on these 'emerging' risk factors in subjects with Normal Glucose Tolerance [NGT]. Therefore, we examined whether elevations of leukocyte count and hsCRP exhibit any association with cardiovascular risk factors and metabolic syndrome in Asian Indian subjects

Madras Diabetes Research Foundation and Dr. Mohan's Diabetes Specialities Centre, Gopalapuram, Chennai, India.
Received : 22.9.2008 Accepted : 29.11.2008
#Rapid Publication

with NGT.

Research Design And Methods

Study subjects were recruited from the Chennai Urban Rural Epidemiology Study (CURES), an ongoing epidemiological study conducted on a representative population (aged ≥ 20 years) of Chennai (formerly Madras), the fourth largest city in India. The methodology of the study has been published elsewhere.[18] Briefly, in Phase 1 of the urban component of CURES, 26,001 individuals were recruited based on a systematic random sampling technique, which is described in our website www.drmohansdiabetes.com (under the link "Publications"). Fasting capillary blood glucose was determined using a One Touch Basic glucose meter (Life scan, Johnson & Johnson, Milpitas, California, USA) in all subjects. Subjects were classified as 'known diabetic subjects' if they stated that they had diabetes and were on the treatment.

In Phase 2 of CURES, all the known diabetic subjects (n=1529) were invited to the centre for detailed studies on vascular complications, and 1382 responded [response rate 90.3%]. From the rest of the study subjects, 10% of newly diagnosed diabetic subjects (n = 320; response rate, 98.8%), 15% of subjects with impaired fasting glucose (n = 866; response rate, 99.1%), and 10% of subjects with normal fasting glucose (n = 1494; response rate, 97.0%) were recruited. Those who were confirmed by OGTT to have 2hour post glucose value < 7.8 mmol/L [140 mg/dl] based on WHO consulting group criteria[19] were labeled as 'normal glucose tolerance' [NGT]. A subset of subjects with NGT [n=1000] were randomly selected to participate in this study and 865 responded [response rate: 86.5%]. The inclusion criteria were: absence of infectious or inflammatory diseases and not on statins or aspirin. Institutional ethical committee approval was obtained for the study and informed consent was obtained from all study subjects.

Anthropometric measurements

Anthropometric measurements including weight, height and waist measurements were obtained using standardized techniques as detailed elsewhere.[18] The body mass index (BMI) was calculated using the formula, weight (kg) / height (m^2). Blood pressure was recorded in the sitting position in the right arm to the nearest 2mm Hg with a mercury sphygmomanometer (Diamond Deluxe BP apparatus, Pune, India). Two readings were taken 5 minutes apart and the mean of the two was taken as the blood pressure.

Biochemical parameters

Fasting plasma glucose (glucose oxidase-peroxidase method), serum cholesterol (cholesterol oxidase-peroxidase-amidopyrine method) serum triglycerides (glycerol phosphate oxidase-peroxidase-amidopyrine method) and HDL cholesterol (direct method-polyethylene glycol-pretreated enzymes) were measured using Hitachi-912 Autoanalyser (Hitachi, Mannheim, Germany). The intra and inter assay co-efficient of variation for the biochemical assays ranged between 3.1% to 7.6%. Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula. Glycated haemoglobin (HbA_1C) was estimated by high-pressure liquid chromatography using the Variant machine (Bio-Rad, Hercules, Calif., USA). The intra and inter assay co-efficient of variation of HbA_1C was <10%.

Measurement of hsCRP and Leukocyte count

The plasma concentrations of hsCRP were measured, in a subset of 192 subjects, by a high sensitive nephelometric assay using a monoclonal antibody to CRP coated on polysterene beads (Dade Behring, Marburg, Germany). The intra-assay and the inter-assay co-efficient of variation for hs-CRP were 4.2% and 6.8 % respectively and the lower detection limit was 0.17 mg/l. Leukocyte count was assessed using flowcytometry [Sysmex – SF3000, Japan]. The intra and inter assay co-efficient of variation of leukocyte count was <10%.

Definitions and diagnostic criteria

Metabolic abnormalities: Hypercholesterolaemia [serum cholesterol ≥ 200 mg/dl or subjects who self reported hypercholesterolemia and were on statins], hypertriglyceridaemia [serum triglycerides ≥ 150 mg/dl or subjects who self reported hypertriglyceridemia and were on drugs for hypertriglyceridemia] and low HDL cholesterol [males: HDL cholesterol <40 mg/dl, females: HDL cholesterol <50 mg/dl] were diagnosed based on ATPIII guidelines.[20] Metabolic syndrome was diagnosed based on modified ATPIII guidelines,[20] if any three of the following abnormalities were present: abdominal obesity [defined as waist circumference ≥ 90 cm for males and ≥ 80 cm for females according to modified Asia Pacific WHO guidelines,[21] high blood pressure [systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85mmHg or subjects who self reported hypertension and were on antihypertensives], hypertriglyceridaemia or low HDL cholesterol. Insulin resistance was calculated using the homeostasis assessment model (HOMA-IR) using the formula: fasting insulin (Iu/mL) fasting glucose (mmol/L)/22.5.

Statistical analysis

Student's t test or one-way ANOVA [with Tukey's HSD] as appropriate was used to compare groups for continuous variables and Chi-square test or Fisher's Exact test as appropriate was used to compare proportions. Study subjects were categorized into tertiles of leukocyte count; unequal numbers were found in the tertiles, due to decimals. Pearson's correlation analysis was carried out to determine the correlation of leukocyte count and hsCRP with cardiovascular risk factors. Logistic regression analysis was carried out using MS as the dependent variable and other risk factors as independent variables. All analysis was done using Windows-based SPSS statistical package (Version 10.0, Chicago) and p values <0.05 were taken as significant.

Results

The clinical and biochemical characteristics of the study

subjects stratified according to tertiles of leukocyte count are shown in Table 1. Body mass index, waist circumference, systolic and diastolic blood pressure, fasting plasma glucose, HbA_1c, serum cholesterol, LDL cholesterol, HOMA IR and hsCRP increased significantly with increasing tertiles of leukocyte count [p for trend <0.001].

Table 2 presents the results of the Pearson's correlation analysis of leukocyte count and hsCRP with cardiovascular risk factors. Leukocyte count had a positive associated with body mass index [p<0.001], waist circumference [p<0.001], systolic and diastolic blood pressure [p<0.01], fasting plasma glucose [p=0.02], HbA_1c [p=0.003], serum cholesterol [p<0.001], triglycerides [p=0.006], LDL cholesterol [p<0.001] and HOMA IR [p<0.001] and a negative association with HDL cholesterol [p=0.04]. hsCRP was positively associated with body mass index [p<0.001], waist circumference [p=0.004], systolic blood pressure [p=0.02], fasting plasma glucose [p=0.003], HbA_1c [p=0.002] and HOMA IR [p=0.002].

In multiple linear regression analysis, hsCRP showed an association with leukocyte count [β =0.131, p=0.008] even after adjusting for age and gender [β =0.128, p=0.011].

Mean levels of leukocyte count and hsCRP in subjects with and without varying metabolic abnormalities are presented in Table 3. Leukocyte count was higher in subjects with abdominal obesity [p<0.001], hypertriglyceridemia [p=0.011], low HDL cholesterol [p=0.002] and metabolic syndrome [p<0.001] compared to their counterparts without the respective metabolic abnormalities.

Subjects with abdominal obesity [p=0.003] and MS [0.04] had significantly higher levels of hsCRP compared those without these abnormalities. Though mean hsCRP levels were higher in subjects with elevated fasting plasma glucose, hypertriglyceridemia, low HDL cholesterol and hypertension compared to their counterparts with normal levels of respective parameters, the differences did not reach statistical significance.

There was a linear increase in the mean values of leukocyte count with increase in number of components of MS [p for trend <0.001] [Fig. 1]. hsCRP levels also increased with increase in number of components of MS [no metabolic abnormality: 1.3 ± 0.5, one metabolic abnormality: 1.9 ± 1.0, two metabolic abnormalities: 2.2 ± 1.1 , ≥ 3 metabolic abnormalities: 2.7 ± 1.4 mg/L] [p for trend <0.001] [Fig. 2].

Logistic regression analysis using MS as dependant variable showed that leukocyte count had a strong association with MS [Odds Ratio (OR): 1.27, 95% confidence interval (CI): 1.14 – 1.42, p<0.001]. This association remained statistically significant even after adjustment for age and

Table 1 : Clinical characteristics of study subjects in tertiles of leukocyte count

Parameters	1st Tertile [n= 288]	2nd Tertile [n= 289]	3rd Tertile [n= 288]
Leukocyte count [x10³/ml]	3.15 – 6.48	6.49 – 7.89	>7.9
Age [years]	39 ± 13	40± 12	41± 12
Male n [%]	144 [50.0]	120 [42.0]	92 [31.9]
Body mass index [kg/m²]	22 ± 4.0	24 ± 4.0**	25 ± 5.0**#
Waist circumference [cm]	82.1 ± 11.3	85.2 ± 10.8**	85.8 ± 12.1**
Systolic blood pressure [mm Hg]	115 ± 14	119 ± 17**	120 ± 17**
Diastolic blood pressure [mm Hg]	73 ± 10	75 ± 10*	76 ± 10**
Fasting plasma glucose [mg/dl]	84 ± 8	85 ± 8	86 ± 9*
HbA_1c [%]	5.5 ± 0.4	5.6 ± 0.4	5.6 ± 0.5*
HOMA IR	1.5 ± 1.0	1.9 ± 1.2**	2.0 ± 1.3**
Total cholesterol [mg/dl]	171 ± 35	181 ± 37**	183 ± 38**
Serum triglycerides [mg/dl]	110 ± 64	116 ± 70	121 ± 62
LDL cholesterol [mg/dl]	105 ± 29	114 ± 32**	116 ± 32**
HDL cholesterol [mg/dl]	45 ± 12	43 ± 9	43 ± 9
HsCRP [mg/L] ^ [n= 192]	1.08 [n= 59]	1.14 [n= 65]	1.82*#@ [n= 68]

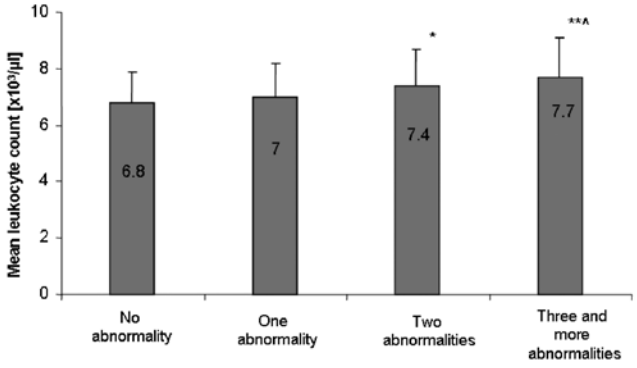
^ Geometric mean. * P<0.01, ** P<0.001 compared to 1st tertile of leukocyte count. # p<0.05 compared to 2nd tertile of leukocyte count. @

Table 2 : Pearson correlation analysis of leukocyte count and hsCRP with cardiovascular risk variables

	Leukocyte count		HsCRP	
value	r value	p value	r value	p
Age	0.019	0.582	0.031	0.671
Body mass index [BMI]	0.200	<0.001	0.326	<0.001
Waist circumference	0.137	<0.001	0.212	0.004
Systolic blood pressure	0.106	<0.01	0.161	0.026
Diastolic blood pressure	0.096	<0.01	0.010	0.888
Fasting plasma glucose	0.079	0.020	0.215	0.003
HbA_1c	0.103	0.003	0.227	0.002
HOMA IR	0.167	<0.001	0.224	0.002
Serum cholesterol	0.150	<0.001	0.058	0.420
Serum triglycerides	0.094	0.006	0.024	0.739
HDL cholesterol	- 0.069	0.044	- 0.087	0.230
LDL cholesterol	0.159	<0.001	0.113	0.118
hsCRP	0.190	0.008	-	-

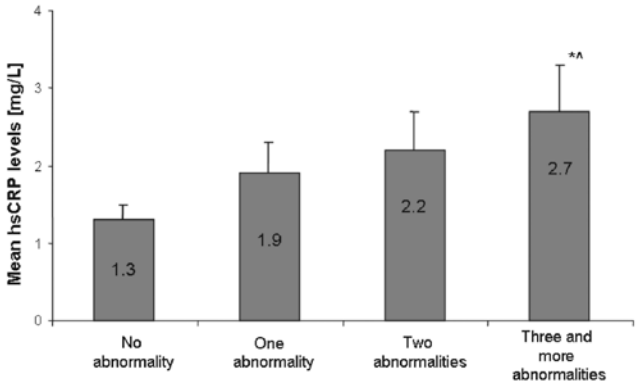
Table 3 : Mean levels of leukocyte count and hsCRP with metabolic abnormalities

Metabolic abnormalities		Mean leukocyte count [x10³/ml]	P value	Mean HsCRP [mg/L]	P value
Abdominal obesity	Present	7.5 ± 1.5	< 0.001	2.6 ± 2.2	0.003
	Absent	7.0 ± 1.4		1.6 ± 1.1	
Hypertension	Present	7.4 ± 1.4	0.113	2.3 ± 1.9	0.647
	Absent	7.2 ± 1.3		2.1 ± 1.6	
Hypertrigly-ceridemia	Present	7.5 ± 1.6	0.011	2.5 ± 1.9	0.308
	Absent	7.2 ± 1.5		2.1 ± 1.5	
Low HDL cholesterol	Present	7.4 ± 1.5	0.002	2.3 ± 1.9	0.159
	Absent	7.1 ± 1.4		1.9 ± 1.5	
Metabolic syndrome	Present	7.7 ± 1.5	< 0.001	2.7 ± 2.1	0.04
	Absent	7.1 ± 1.4		2.0 ± 1.5	



Error bars indicate SD. *p<0.01, *p<0.001 compared to no abnormality. ^p for trend <0.001

Fig.1: mean Leukocyte count in relation to number of metabolic abnormalities.



Error bars indicate SD. *p<0.01 compared to no abnormality. ^p for trend <0.001

Fig. 2 : Mean hsCRP in relation to number of metabolic abnormalities.

gender [OR: 1.28, 95% CI: 1.15 – 1.44, p<0.001]. hsCRP was significantly associated with MS [Odds Ratio (OR): 1.14, 95% confidence interval (CI): 1.00 – 1.32, p=0.04]. This association remained statistically significant even after adjusting for age and gender [OR: 1.16, 95% CI: 1.01 – 1.34, p=0.03] [Table 4].

Discussion

The main findings of the study are that in Asian Indian subjects with NGT, both leukocyte count and hsCRP show an association with most cardiovascular risk factors and MS.

Earlier studies in the west have reported that leukocyte count and hsCRP are associated with MS, diabetes and CAD.[6,7,10,11,17] This is the first study however to report on the association of both leukocyte count and hsCRP with cardiovascular risk factors and MS in an Asian Indian population and is significant because of the high prevalence of insulin resistance, diabetes and premature CAD in this ethnic group.[2,22]

The contributory role of inflammatory markers in cardiovascular disease has been documented in several studies. Abdominal obesity is considered to be the main link between inflammation and metabolic disorders. Leukocyte count has been demonstrated to be associated with abdominal obesity in Pima Indians, Whites and Blacks.[23] Similarly, several studies have shown an association of hsCRP with abdominal obesity.[17,24] This led to the suggestion that both leukocyte count and hsCRP play a major role in linking adiposity to diabetes and CAD. Our results corroborate these findings as both leukocyte count and hsCRP had a significant association with waist circumference. These data also support the hypothesis that subclinical inflammation could perhaps be a component of metabolic syndrome.

Table 4 : Multiple logistic regression analysis

Parameter	Dependent variable: Metabolic syndrome Odds Ratio [OR]	95% Confidence Interval [CI]	P value
Leukocyte count			
Unadjusted	1.27	1.14 – 1.2	<0.001
Adjusted for age	1.28	1.14 – 1.43	< 0.001
Adjusted for age and gender [Male=0, Female=1]	1.28	1.15 – 1.44	< 0.001
HsCRP			
Unadjusted	1.14	1.00–1.32	0.04
Adjusted for age	1.16	1.00 – 1.34	0.03
Adjusted for age and gender [Male=0, Female=1]	1.16	1.01 – 1.34	0.03

Earlier studies have reported that leukocyte count and hsCRP are increased in subjects with MS.[13] In the CARDIA study, a significant positive association was observed between leukocyte count and systolic blood pressure and BMI, and a negative correlation with HDL-cholesterol.[25] Our results are in agreement with these findings. We also observed that body mass index and systolic blood pressure increased, while HDL cholesterol decreased with increase in tertiles of leukocyte count.

Targher et al[26] investigated the association between leukocyte count and CAD risk factors, and reported that a higher leukocyte count was associated with clustering of components of metabolic syndrome. Similar results were observed in the present study in which both leukocyte count and hsCRP were increased in subjects with MS. We also observed that both showed a significant association with MS even after adjusting for age and gender. This indicates that normal subjects having increasing levels of both leukocyte count and hsCRP are more prone to cardiovascular risk.

It was also observed that both leukocyte count and hsCRP increased with increase in number of metabolic abnormalities indicating a dose–response relationship between these risk factors and metabolic abnormalities. This relationship also suggests that subjects with a single MS component could have low-grade inflammation, which might intensify as the number of MS components increase. Similar results were found in a study on Japanese men, which reported that leukocyte count increased with increase in number components of MS.[27]

Although the mechanism by which the leukocyte

count is linked to MS remains unclear, there are several explanations. It has been suggested that the link could be through insulin resistance, which predisposes one to diabetes, MS and CAD.[3] In this context, it is important note in our study that insulin resistance increased with increase in tertiles of leukocyte count. The mechanism underlying the strong relationship between leukocyte count and insulin resistance may be a subtle activation of the immune system, leading to increased expression of proinflammatory factors shown strongly associated with insulin resistance. Another explanation for the link between leukocyte and MS could be through vascular endothelial cells. Vascular endothelial cells are activated by the presence of atherosclerotic risk factors, such as hypertension, hyperlipidemia and hyperglycemia. Endothelial cells produce intracellular adhesion molecule - 1, an adhesion molecule, which causes leukocyte to adhere to the vascular wall, after which they can penetrate the vascular endothelium and produce new cytokines and chemokines. Cytokines then activate the leukocyte and cells comprising the vascular wall, promoting platelet aggregation and thrombus formation.[28] Proinflammatory cytokines are also known to increase the leukocyte count, which in turn could further exacerbate the inflammation. Further studies are necessary to elucidate the role of leukocytes and hsCRP in the mechanisms underlying MS.

One of the limitations of our finding is that being a cross-sectional study, a cause-and-effect relation of leukocyte count and hsCRP with metabolic syndrome cannot be determined. However the strength of the study is that it is a population-based study and the first in Asian Indians who are a high risk group for both diabetes and CAD.

In conclusion, this study reports that among Asian Indians who are known to have high risk of premature coronary artery disease and diabetes, a significant association exists between both leukocyte count and hsCRP with metabolic syndrome and cardiovascular risk factors even among non-diabetic subjects. This study is significant because in developing countries like India where hsCRP measurement could be more expensive, even a simple leukocyte count - which represents systemic inflammation, could serve as a risk marker for cardiovascular disease, if infections were excluded.

Acknowledgement

The authors wish to thank the Chennai Willingdon Corporate Foundation for their support for the CURES field studies. This is the 64th paper from Chennai Urban Rural Epidemiology Study (CURES).

References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes, estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
2. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. Circulation 1998;97:596–601.
3. Reaven GM. Role of insulin resistance in human disease (syndrome X): an expanded definition. Annu Rev Med 1993;44:121-31.
4. Weijenberg MP, Feskens EJ, Kromhout D. White blood cell count and the risk of coronary heart disease and all-cause mortality in elderly men. Arterioscler Thromb Vasc Biol 1996;16:499-503.
5. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342:836-43.
6. Brown DW, Giles WH, Croft JB. White blood cell count: an independent predictor of coronary heart disease mortality among a national cohort. J Clin Epidemiol 2001;54:316–22.
7. Ernst E, Hammerschmidt DE, Bagge U, Matrai A, Dormandy JA. Leukocytes and the risk of ischemic diseases. JAMA 1987;257:2318-24.
8. Murohara T, Buerke M, Lefer AM. Polymorphonuclear leukocyte-induced vasocontraction and endothelial dysfunction: role of selectins. Arterioscler Thromb 1994;14:1509-19.
9. Elkind MS, Cheng J, Boden-Albala B, Paik MC, Sacco RL. Elevated white blood cell count and carotid plaque thickness: the Northern Manhattan Stroke Study. Stroke 2001;32:842-49.
10. Vozarova B, Weyer C, Lindsay RS, Pratley RE, Bogardus C, Tataranni PA. High white blood cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes. Diabetes 2002;51:455-61.
11. Ridker PM, Rifai N, Pfeffer MA, Sacks FM, Moye LA, Goldman S, Flaker GC, Braunwald E. Inflammation, pravastatin, and the risk of coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events (CARE) Investigators. Circulation 1998;98:839-44.
12. Albert MA, Glynn RJ, Ridker PM. Plasma concentration of C reactive protein and the calculated Framingham coronary heart disease risk score. Circulation 2003;108:161-65.
13. Ridker PM, Wilson P, Grundy SC. Should C-Reactive Protein be added to metabolic syndrome and to assessment of global cardiovascular risk? Circulation 2004;109:2818-25.
14. Haverkate F, Thompson SG, Pyke SD, Gallimore JR, Pepys MB. 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 1997;349:462-66.
15. Ford ES. Body mass index, diabetes, and C-reactive protein among U.S. adults. Diabetes Care 1999;22:1971-77.
16. Murray CJ, Lopez AD. Alternative projection of mortality and disability by cause 1990-2020; Global Burden of Disease Study. Lancet 1997;349:1498-1504.
17. Mohan V, Deepa R, Velmurugan K, Premalatha G. Association of C-reactive protein with body fat, diabetes and coronary artery disease in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-6). Diabet Med 2005;22: 863-70.
18. Deepa M, Pradeepa R, Rema M, Mohan A, Deepa R, Shanthirani S, Mohan V. The Chennai Urban Rural Epidemiology Study (CURES)—study design and methodology (urban component) (CURES-I). J Assoc Physicians India 2003;51:863-70.
19. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus, provisional report of a WHO Consultation. Diabet Med 1998;15:539-53.
20. Grundy SM, Cleeman JI, Merz CN, et al. National Heart, Lung, and Blood Institute; American College of Cardiology Foundation; American Heart Association. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. Circulation 2004;110:227-39.
21. The Asia Pacific perspective: Redefining obesity and its treatment. Regional Office for the Western Pacific of the World Health Organization. World Health Organization, International Association for the Study of Obesity and International Obesity Task Force. Health Communications Australia Pty Limited, Sydney. 2000;17-21.
22. Mohan V, Deepa R, Shanthirani S, et al. Prevalence of coronary artery disease and its relationship to lipids in a selected population in South

India – The Chennai Urban Population Study - 5. J Am Coll Cardiol 2001;38:682-687

23. Pratley RE, Wilson C, Bogardus C. Relation of the white blood cell count to obesity and insulin resistance: effect of race and gender. Obesity Research 1995;3:563–71.
24. Lemieux I, Pascot A, Prud'homme D, Almeras N, Bogaty P, Nadeau A, et al. Elevated C-reactive protein: another component of the atherothrombotic profile of abdominal obesity. Arterioscler Thromb Vasc Biol 2001;21:961–67.
25. Friedman GD, Tekawa I, Grimm RH, Manolio T, Shannon SG, Sidney S. The leucocyte count: correlates and relationship to coronary risk factors: the CARDIA study. Int J Epidem 1990;19:889–93.
26. Targher G, Seidell JC, Tonoli M, Muggeo M, De Sandre G, Cigolini M. The white blood cell count: its relationship to plasma insulin and other cardiovascular risk factors in healthy male individuals. J Intern Med 1996;239:435-41.
27. Nagasawa N, Tamakoshi K, Yatsuya H, Hori Y, Ishikawa M, Murata C, Zhang H, Wada K, Otsuka R, Mabuchi T, Kondo T, Toyoshima H. Association of white blood cell count and clustered components of metabolic syndrome in Japanese men. Circ J 2004;68:892-97.
28. Ross R. Atherosclerosis: An inflammatory diesase. N Engl J Med 1999;340:115-26.

Announcement

JAPI Judges for Best Paper Award

I am extremely grateful to the Judges: Dr. AL Kakrani (Pune), Dr. DK Kochar (Bikaner), Dr. TK Suma (Alappuzha), Dr. Ajay Kumar (Patna), and Lt Col (Dr.) Rajat Kumar (New Delhi) for their painstaking efforts put by them while evaluating all articles published during the year 2008.

Dr. Shashank R Joshi,
Hon. Editor, JAPI.

Announcement

VR Joshi JAPI Award for Outstanding Referee for the year 2008

Dr. Shyam Sundar (Varanasi)

Dr. Zarir Udwadia (Mumbai)

Dr. AG Unnikrishnan (Kochi)

Dr. Shashank R Joshi,
Hon. Editor, JAPI.