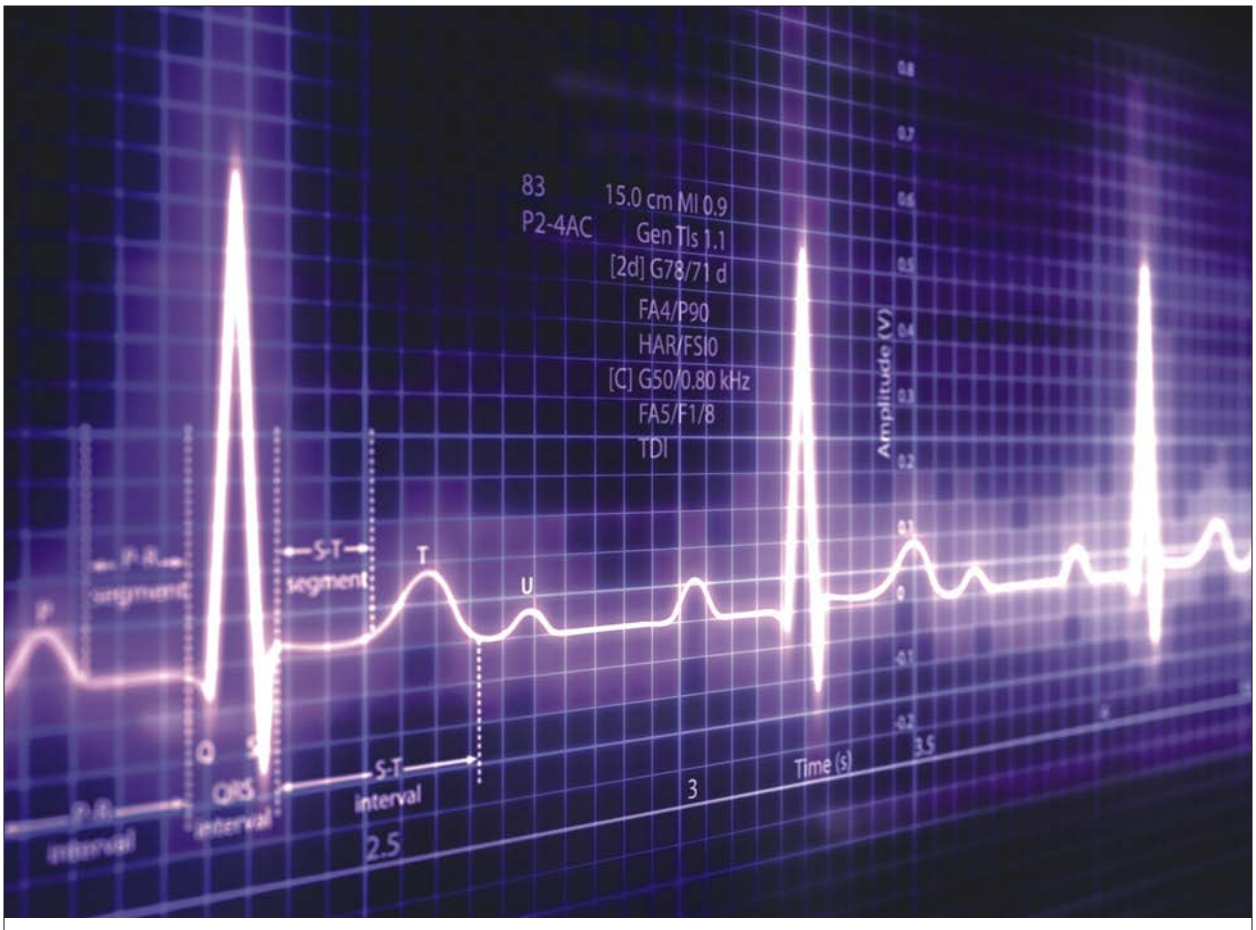

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Homocysteine Level and Cardiovascular Afflictions in the Black African Patients in Lome

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Abstract: The goal of the present study was to analyze the relationship between homocysteinemia and cardiovascular afflictions in African patients. This prospective study was performed at the Department of Cardiology in the Campus Teaching Hospital of Lomé, from March 1 to November 30, 2008. All patients benefited from a complete cardiovascular evaluation and an assessment of blood homocysteine levels. The prevalence of hyperhomocysteinemia was 45.6%. Age ($r = +0.099$, $p<0.0001$), but not sex, was correlated with homocysteinemia. In contrast, body mass index ($r = - 0.247$, $p<0.0001$) was negatively linked to homocysteinemia. Both systolic arterial pressure ($r = +0.064$, $p<0.0001$) and diastolic arterial pressure ($r = +0.148$, $p<0.0001$) also demonstrated a correlation. Among all of the cardiovascular afflictions, the ischemic heart diseases ($r = +0.153$, $p<0.0001$) had the strongest association with homocysteinemia. The prevalence of hyperhomocysteinemia was very high among the cardiovascular patients in Togo. This hyperhomocysteinemia was correlated with high blood pressure and ischemic heart diseases, which are becoming more prevalent in this part of the world. The management of this new risk factor, which is based mainly upon its prevention, has been shown to be essential and must become a major public health issue.

Key words: Homocysteinemia, cardiovascular affliction, correlation

INTRODUCTION

For more than three decades, hyperhomocysteinemia has been considered to be an independent risk factor for obstructive cardiovascular pathologies (Guilland *et al*., 2003). The numerous epidemiological and clinical studies that have been performed in the developed countries have produced contradictory results. Some of those studies (Ueland *et al*., 2000; Brattstrom and Wilcken, 2000) have demonstrated a relationship between moderate hyperhomocysteinemia and the thromboembolic and ischemic cardiovascular diseases (CVD) (Nevado Jr. and Imasa, 2008). Other studies, however, have shown that high homocysteine levels in populations that are free of the traditional risk factors, such as High Blood Pressure (HBP), diabetes, dyslipidemia, smoking status and obesity, did not result in an increase in the number of morbid cardiovascular events (Alfthan *et al*., 1994; Evans *et al*., 1997), suggesting that hyperhomocysteinemia can have a contributing role only in the presence of other cardiovascular risk factors. Another theory proposed that hyperhomocysteinemia that is found in CVD patients might actually be a consequence of these thromboembolic and ischemic CVDs (Guilland *et al*., 2003).

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Currently, the measurement of blood homocysteine levels is included in the screening tests for patients who suffer from premature obstructive cardiovascular pathologies (David, 2000), particularly for those patients without any known traditional cardiovascular risk factors. Those individuals who are found to have elevated blood levels are prescribed a vitamin regimen that includes vitamins B6, B9 and B12 (Wang *et al*., 2007) in order to reduce homocysteine levels. However, this treatment does not reduce the risk of arisen of cardiovascular events in patients with a high cardiovascular risk (Ray *et al*., 2007; Ebbing *et al*., 2008; Imasa *et al*., 2009).

In the sub-Saharan African countries in general and particularly in Togo, studies in this field are rare. This study was focused on the following major aims: (1) to determine the prevalence of hyperhomocysteinemia in our patient population, (2) to evaluate the relationship between homocysteinemia and other cardiovascular risk factors and (3) to evaluate the relationship between homocysteinemia and the type of CVD.

MATERIALS AND METHODS

Study Population

This study was performed at the Department of Cardiology in the Campus University Teaching Hospital, which is the second national reference hospital in Togo. This prospective study included 114 cardiovascular patients of African descent (Table 1) who were admitted or seen on an out-patient basis between March 1, 2008 and November 30, 2008 and who were tested for the level of homocysteine. After inclusion in the study, each patient received a questionnaire that was used to obtain information regarding sex, age and CVD diagnosis.

The types and frequencies of CVDs in the patient population are presented in Table 1. For purposes of this study, the following criteria were used:

- Ischemic heart disease was defined by the presence of one of the following: angina pectoris, as characterized by chest pain during exercise that is improved by rest or trinitrin and confirmation by electrocardiogram (ECG); myocardial infarction; or diagnosis based upon typical ECG signatures
- Cerebrovascular stroke was defined by the following, with the diagnosis confirmed by CT scan: transitory ischemic attack, thrombotic stroke or haemorrhagic stroke
- Venous thrombo-embolic disease was defined by the association of all of the following features: clinical signs, including pain and oedema of the lower limbs, a decrease in venous blood flow and the positive identification by Doppler echography of a thrombus in a vein in the lower limbs
- Obliterant chronic arteriopathy of the lower limbs was defined by a decrease in the arterial blood flow through the lower limbs, which may be associated with a plate of atheroma, as diagnosed by the Doppler echography

Table 1: Distribution of patients according to CVD at inclusion

Cardiovascular disease	n (%)
High Blood Pressure (HBP)	38 (33.4)
Venous thrombo-embolic disease	19 (16.7)
Ischemic cerebro-vascular stroke	18 (15.8)
Ischemic cardiac disease	13 (11.4)
Cardiac failure	16 (14.0)
Metabolic syndrome	3 (2.6)
Hemorrhagic cerebral stroke	3 (2.6)
Obliterant chronic arteriopathy of the lower limbs	4 (3.5)
Total	114 (100)

- Cardiac failure was defined by clinical signs and confirmation by Doppler echocardiography.

The Body Mass Index (BMI) was calculated for each patient. The patients were classified into three groups: obese patients, with BMI≥30 kg m^{-2}; overweight patients, with 25 kg m^{-2}≤BMI≤30 kg m^{-2} and normal weight patients, with BMI is <25 kg m^{-2}.

A patient was considered to be hypertensive if the systolic blood pressure ≥18664.8 Pa (140 mmHg) or the diastolic blood pressure ≥11998.8 Pa (90 mmHg). The supine blood pressure in both two arms was measured by a nurse using a manual sphygmomanometer (Mancia *et al*., 2007). After a ten-minute rest period, the blood pressure was measured three times and the mean of the last two measurements was considered to be the patient's blood pressure.

Measurement of Blood Homocysteine Levels

Blood samples were taking during fasting. The level of homocysteine was measured by the immunological technique of fluorescence polarization using the AxSYM system. Normal values ranged between 5 and 15 μmol L^{-1}. Hyperhomocysteinemia was defined as homocysteine levels that were greater than 15 μmol L^{-1} (Demuth *et al*., 2000) and patients with hyperhomocysteinemia were further classified into three groups: moderate hyperhomocysteinemia, with homocysteine levels between 16 and 30 μmol L^{-1}; intermediate hyperhomocysteinemia, with homocysteine levels between 31 and 100 μmol L^{-1} and severe hyperhomocysteinemia, with homocysteine levels greater than 100 μmol L^{-1} (Demuth *et al*., 2000). The level of homocysteine was correlated with several physical and clinical characteristics, including age, sex, BMI and type of CVD.

Data Analysis

All quantitative parameters are presented as the average±mean deviation and all qualitative parameters are presented as the number and its corresponding percentage. The distribution (casting) of the qualitative parameters was analyzed by the chi square test.

For the multivariate analysis, the coefficient of correlation was calculated using Excel software v. 2003. The student's t-test was used to verify the results (estimation of error margin), with a significance threshold of 0.05.

Associations between variables were considered to be great if the coefficient was greater than 0.5, to be average if the coefficient was between 0.5 and 0.2 and to be low if the coefficient was less than 0.2. The absence of correlation between variables was determined if the coefficient was less than 0.001.

The treatment and analyses of the data were performed using the software programs Epi-Info v. 6.04 and Microsoft Excel v. 2003.

RESULTS

Age and Sex

The study included a total of 114 patients, with 43 (37.7%) men and 71 (62.3%) women. The sex ratio was 0.60. The average age was 53±15.5 years old (range = 17-90 years).

The average homocysteinemia was 18.7±19.6 μmol/l (range = 6.1-194.9 μmol L^{-1}) statistically non significant difference between the sexes with respect to homocysteine levels (male average = 18.7±11.4 μmol L^{-1}, female average = 18.7±23.2 μmol L^{-1}; p = 0.995). Fifty-two (45.6%) patients had hyperhomocysteinemia and, of these, twenty-one (48.8%) were male and thirty-one (42.9%) were female (p = 0.590). Further classification revealed that

42 (36.8%) patients had moderate hyperhomocysteinemia, 9 (7.9%) had intermediate hyperhomocysteinemia and 1 (0.9%) had severe hyperhomocysteinemia. There was no significant association between age and homocysteine levels (p = 0.11) (Table 2).

Systolic and Diastolic Arterial Pressure

The average systolic blood pressure was 151.6±32.5 mmHg (range = 90-280 mmHg) and the average diastolic blood pressure was 92.3±16.5 mmHg (range = 60-150 mmHg). Seventy seven (67.6%) patients were hypertensive (Table 3); 40 of them (51.9%) had hyperhomocysteinemia against 37 (32.2%) whose homocysteine levels was normal.

Body Mass Index (BMI)

The average BMI was 27.4±5.3 kg m^{-2} (range = 16.0-50.1 kg m^{-2}). The average homocysteinemia was 25.1±30.7 μmol L^{-1} (range = 6.1 - 194.9 μmol L^{-1}) in patients with normal BMI, 14.8±6.1 μmol L^{-1} (range = 6.4-34.9 μmol L^{-1}) in overweight patients and 15.7±64 μmol L^{-1} (range = 6.5-38.6 μmol L^{-1}) in obese patients. The average homocysteinemia was significantly different between the three weight groups (p = 0.030). There was statistically no significant difference in the percentage of patients with high homocysteine levels according to the BMI classes, p = 0.41 (Table 4).

Lipid and Sugar Levels in Blood

The average total cholesterol level in blood was 2.1±0.7 g L^{-1} (range = 0.5 - 4.3 g L^{-1}), with an average LDL-cholesterol level of 1.4±0.4 g L^{-1} (range = 0.1 - 3.1 g L^{-1}) and an average HDL-cholesterol level of 0.4±0.2 g L^{-1} (range = 0.1 - 1.4 g L^{-1}). The average triglyceride level in blood was 1.4±0.8 g L^{-1} (range = 0.4 - 4.9 g L^{-1}).

Twenty-five (21.9%) patients were diabetics (Table 5); the average glycaemia was 1.2±0.6 g L^{-1}(range = 0.58 - 4.57 g L^{-1}).

Table 2: Homocysteinemia according to age

Age (years)	No. (%)	Hcy (A)<5 μmol L^{-1} n (%)	Hcy (A)>5 μmol L^{-1} n (%)
<30	8 (7)	5 (62.5)	3 (37.5)
30-59	67 (58.8)	41 (61.2)	26 (38.8)
= 60	39 (34.2)	16 (41)	23 (59)

Hcy (A) = Homocysteine level in the blood

Table 3: Homocysteine level according to the blood pressure

Levels	Hcy (A)<5 μmol L^{-1} n (%)	Hcy (A)>5 μmol L^{-1} n (%)	Total
Hypertensive	37(32.5)	40 (35.1)	77 (67.6)
Non hypertensive	25 (21.9)	12 (10.5)	37 (32.4)
Total	62 (54.4)	52 (45.6)	114 (100)

Hcy (A) = Homocysteine level in the blood ; p = 0.05

Table 4: Hyperhomocysteinemia according to BMI

BMI	Number	Hyperhomocysteinemia n (%)
Normal	41	22 (53.7)
Over weight	43	17 (39.5)
Obese	30	13 (43.3)

p = 0.41

Table 5: Homocysteine level according to the glycaemia

Levels	Average Hcy m±ET (μmol L^{-1})	Hcy (A)<5 μmol L^{-1} n (%)	Hcy (A)>5 μmol L^{-1} n(%)	Total
Diabetics	16.1±6.1	12 (10.5)	13 (11.4)	25 (21.9)
Non diabetics	20.2±23.8	25 (34.2)	50 (43.9)	89 (78.1)
Total	18.7 ± 19.6	51 (447)	63 (55.3)	114 (100)

Hcy (A) = Homocysteine level in the blood; p = 0.479

Table 6: Cardiovascular risk factors and obstructive cardiovascular pathologies correlated with homocysteinemia

Cardiovascular risk factors and pathologies	Coefficient of correlation (r)	Index of student's t test (p)
High blood pressure	+0.109	p<0.0001
Age	+0.099	p<0.0001
BMI (A)	-0.247	p<0.0001
Systolic arterial pressure	+0.064	p<0.0001
Diastolic arterial pressure	+0.148	p<0.0001
Total cholesterol	-0.239	p<0.0001
HDL cholesterol	-0.174	p<0.0001
LDL cholesterol	-0.235	p<0.0001
Triglycerides	-0.031	p<0.0001
Glycaemia	-0.084	p<0.0001
Ischemic heart disease	+0.153	p<0.0001
Venous thrombo-embolic disease	+0.071	p<0.0001
Ischemic cerebro-vascular stroke	+0.006	p<0.0001
Obliterant chronic arteriopathy of the lower limbs	+0.0.018	p<0.0001

(A) = Body mass index

Coefficients of Correlation

Homocysteinemia was not correlated with sex ($r<0.001$) but was strongly correlated negatively with BMI and the total cholesterol levels (Table 6). Homocysteinemia is positively correlated with age and HBP, whereas it is negatively correlated with the other cardiovascular risk factors. It was also positively correlated with ischemic heart disease.

DISCUSSION

The homocysteine levels in blood were determined for a population of African cardiovascular patients and the levels were analyzed with respect to age, sex, BMI, blood lipid levels, blood sugar level and the type of cardiovascular disease. This study was performed in a cardiology department due to financial constraints and the fact that all hospital patients in Togo are fully responsible for paying for their own laboratory tests, which is in contrast to the systems in some developed countries, such as Belgium, in which homocysteine tests are free for CVD patients younger than 55 years (Girs and Giet, 2006). Because all our subjects were patients, these limitations could have an impact on our results, leading to potential overestimations.

The prevalence of hyperhomocysteinemia was 45.6%, which is comparable to what has been seen in other African countries. The prevalence of hyperhomocysteinemia was reported to be 56% in the West African countries (Amouzou *et al*., 2004) and 41% in Algeria (Hambaba *et al*., 2008). This high prevalence among Africans might potentially be due to the consumption of foods that have low levels of vitamins B6, B9 and B12 as well as a high proportion of individuals with the C677T polymorphism in the *methylene tetrahydrofolate reductase* gene (Amouzou *et al*., 2004). Another potentially confounding factor could be that the reagents and protocols used to measure homocysteine levels are based upon Europeans populations. Thus, a review of the available biological tests, the local diet(s) and the geographical situation will be important areas to examine further.

The observed prevalence in this study is much higher than that found in most of the studies carried out in European countries. In France, the prevalence was 7.5% among a total of 2045 military subjects (Chellak *et al*., 2005). The low prevalence of hyperhomocysteinemia in developed countries might be a result of the more balanced diets that can be found in these populations.

The average homocysteine levels in our study was higher than the levels found in the other studies involving African countries, with 13.5 μmol L^{-1} (Amouzou *et al*., 2004) and

14.69 μmol L^{-1} (Hambaba *et al*., 2008). The typical gap of this study was higher than the average because of the fact that the superior value of our sample was very far away from others values. Our higher average might be a result of the sample population, who were all CVD patients.

Homocysteinemia was positively correlated with age. A greater proportion of older patients had hyperhomocysteinemia than did younger patients (59% vs. 38.8 and 37.5%). These results demonstrate that homocysteinemia increases with age, which can potentially be explained by metabolic failure at advanced ages.

Homocysteinemia was not correlated with sex in this study ($r<0.001$), which is in contrast to the data that can be found in the literature. One potential explanation could involve the size of our patient population.

The average homocysteinemia and the prevalence of hyperhomocysteinemia were higher in normal weight patients than in overweight ones. There was a negative correlation ($r = -0.247$) between homocysteinemia and BMI, indicating that homocysteine levels decreased as weight increased. A similar, although lower, negative correlation ($r = -0.07$) was observed in a population from Great Britain (Whincup *et al*., 1999). One potential explanation is that overweight individuals utilize a larger amount of methionine, which is metabolized into homocysteine, during protein synthesis, thus leading to less available methionine to be converted into homocysteine.

Homocysteinemia was positively correlated with diastolic ($r = +0.148$; $p<0.0001$) and systolic ($r = +0.064$; $p<0.0001$) arterial pressures. These results are similar to those seen in other studies, although they demonstrated a stronger correlation with the diastolic arterial pressure than with the systolic. In one study (Chellak *et al*., 2005), the correlation coefficients for the systolic and diastolic arterial pressure were +0.063 and +0.082, respectively, which indicated that hyperhomocysteinemia causes a greater increase in diastolic arterial pressure than in systolic arterial pressure.

Homocysteinemia was negatively correlated with the four parameters of lipid analysis (Total cholesterol: $r = -0.239$; $p<0.0001$, LDL cholesterol: $r = -0.235$; $p<0.0001$, HDL cholesterol: $r = -0.174$; $p<0.0001$, triglycerides: $r = -0.031$; $p<0.0001$). It was also negatively correlated with the glycaemia. This observation is consistent with other studies. One such study (Bostom, 1999) found negative correlations between homocysteinemia and HDL cholesterol ($r = -0.114$) and total cholesterol ($r = -0.049$). These observations indicate that, as dyslipidemia becomes more severe, the levels of homocysteine become even lower.

Homocysteinemia was more strongly correlated with the ischemic cardiopathies ($r = +0.153$; $p<0.0001$) than each of the following obstructive cardiovascular diseases: venous thrombo-embolic disease ($r = +0.071$; $p<0.0001$), obliterant chronic arteriopathy of the lower limbs ($r = +0.018$; $p<0.0001$) and ischemic cerebro-vascular stroke ($r = +0.006$; $p<0.0001$).

Therefore, hyperhomocysteinemia appears to be more likely associate to ischemic heart disease than any of the obstructive cardiovascular diseases.

CONCLUSION

The prevalence of hyperhomocysteinemia was very high in cardiovascular patients in Togo. This hyperhomocysteinemia is correlated to HBP and to ischemic cardiopathies, which are becoming more prevalent in this part of the world. The management of this new risk factor, which is based primarily on its prevention, has been proven to be essential and should become a major focus of public health. The prevention of hyperhomocysteinemia

should include education of the population, with the objective of changing cooking habits so that foods are not overcooked and changing diet to encourage the consumption of foods that are rich in vitamins B6, B9 and B12.

REFERENCES

Alfthan, G., J. Pekkanen, M. Jauhiainen, J. Pitkaniemi and M. Karvonen *et al*., 1994. Relation of serum homocysteine and lipoprotein(a) concentrations to atherosclerotic disease in a prospective Finnish population based study. Atherosclerosis, 106: 9-19.

Amouzou, E.K., N.W. Chabi, C.E. Adjalla, R.M. Rodriguez-Gueant and F. Feillet *et al*., 2004. High prevalence of hyperhomocysteinemia related to folate deficiency and the 677C?T mutation of the gene encoding methylenetetrahydrofolate reductase in coastal West Africa. Am. J. Clin. Nutr., 79: 619-624.

Bostom, A.G., H. Silbershatz, I.H. Rosenberg, J. Selhub and R.B. D'Agostino *et al*., 1999. Nonfasting plasma total homocysteine levels and all-cause and cardiovascular disease mortality in elderly framingham men and women. Arch. Intern. Med., 159: 1077-1080.

Brattstrom, L. and D.E. Wilcken, 2000. Homocysteine and cardiovascular disease: Cause or effect?. Am. J. Clin. Nutr., 72: 315-323.

Chellak, S., C. Bigaillon, Y. El Jahiri, C. Garcia and F. Ceppa *et al*., 2005. Homocystéine et paramètres du syndrome métabolique et du risque cardiovasculaire chez 2045 militaires: Etude EPIMILcorrelation results between plasma homocysteine, metabolic syndrome components and cardiovascular risk markers in 2045 french military subjects: EPIMIL cohort. Immuno Analyze Biol. Spéc., 20: 169-172.

David, J.L., 2000. Hyperhomocysteinemia, risk factor of venous thrombo-embolic disease?. Louvain Med., 119: 191-196.

Demuth, K., S. Drunat, J.L. Paul and N. Moatti, 2000. Hyperhomocysteinemia and atherosclerosis. Médecine/Science, 16: 1081-1090.

Ebbing, M., O. Bleie, P.M. Ueland, J.E. Nordrehaug and D.W. Nielsen *et al*., 2008. Mortality and cardiovascular events in patients treated with homocysteine-lowering B vitamins after coronary angiography: A randomized controlled trial. JAMA., 300: 795-804.

Evans, R.W., J. Shaten, J.D. Hempel, J.A. Cutler and L.H. Kuller, 1997. Homocysteine and risk of cardiovascular disease in the multiple risk factor intervention trial. Arterioscler. Thromb. Vasc. Biol., 17: 1947-1953.

Girs, N. and D. Giet, 2006. Should general practitioners be interested in homocysteine measurements?. Rev. Med. Liege., 61: 352-361.

Guilland, J.C., A. Favier, G. Potier-de-Courcy, P. Galan and S. Hercberg, 2003. Hyperhomocysteinemia: An independent risk factor or a simple marker of vascular disease? 2. Epidemiological data. Pathol. Biol., 51: 111-121.

Hambaba, L., A. Abdessemed, M. Yahia, S. Laroui and F. Rouabah, 2008. Relationship between hyperhomocysteinemia and C677T polymorphism of methylene tetrahydrofolate reductase gene in a healthy Algerian population. Ann. Biol. Clin., 66: 637-641.

Imasa, M.S., N.T. Gomez and J.B. Jr. Nevado, 2009. Folic acid-based intervention in non-ST elevation acute coronary syndromes. Asian Cardiovasc. Thorac. Ann., 17: 13-21.

Mancia, G., G. De Backer, A. Dominiczak, R. Cifkova, R. Fagard and G. Germano *et al*., 2007. Guidelines for the management of arterial hypertension: The task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J. Hypertens, 25: 1105-1187.

Nevado, Jr. J.B. and M.S. Imasa, 2008. Homocysteine predicts adverse clinical outcomes in unstable angina and non-ST elevation myocardial infarction: Implications from the folate intervention in non-ST elevation myocardial infarction and unstable angina study. Coron. Artery Dis., 19: 153-161.

Ray, J.G., C. Kearon, Q. Yi, P. Sheridan and E. Lonn, 2007. Homocysteine-lowering therapy and risk for venous thromboembolism: A randomized trial. Ann. Intern. Med., 146: 761-767.

Ueland, P.M., H. Refsum, S.A. Beresford and S.E. Vollset, 2000. The controversy over homocysteine and cardiovascular risk. Am. J. Clin. Nutr., 72: 324-332.

Wang, X., X. Qin, H. Demirtas, J. Li and G. Mao *et al.*, 2007. Efficacy of folic acid supplementation in stroke prevention: A meta-analysis. Lancet, 369: 1876-1882.

Whincup, P.H., H. Refsum, I.J. Perry, R. Morris and M. Walker *et al.*, 1999. Serum total homocysteine and coronary heart disease: Prospective study in middle aged men. Heart, 82: 448-454.