

## CORRELATION OF HYPERHOMOCYSTEINEMIA WITH HYPERTENSION

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### ABSTRACT

The association of homocysteine with blood pressure deserves attention because blood pressure may mediate part of the cardiotoxic effect of homocysteine<sup>2,3</sup>. The present study included 40 cases of hypertension and age & sex matched 20 healthy control subjects. They were further divided into 3 groups, Viz: Group-I : With hypertension, Group-II : Hypertension with CAD and Group-III : Hypertension with Type 2 DM. Plasma homocysteine was estimated in both case and control groups by CLIA (Chemiluminescence Immune Assay). Primary objective being study of relationship of plasma homocysteine and hypertension analysis of data shows that mean plasma homocysteine level of  $38.340 \pm 15.250$   $\mu\text{mol/L}$  when compared with systolic blood pressure  $160.1 \pm 13.071$  mmHg has 'p' value  $< 0.05$  and 'r' value 0.6741. This warrants for intervention by homocysteine lowering agents like folic acid, Vit.B-12, Vit.B-6 in addition to control of lipid profile in gaining importance in management of hypertension, CAD and Type 2 DM.

**KEYWORDS:** Folate, Homocysteine, Hypertension, Methionine

### INTRODUCTION

Homocysteine is a sulfur-containing, nonproteinogenic amino acid biosynthesized from methionine that takes a key place between the folate and activated methyl cycles. A causal link between homocysteine and blood pressure is supported by experimental studies. In cell culture studies, homocysteine induced oxidative stress to endothelium and reduced available nitric oxide. Homocysteine may elevate blood pressure through multiple mechanisms, including its effect on vascular endothelial integrity<sup>1,4</sup>.

Recent studies suggest that mild elevations in serum homocysteine may contribute to elevations in blood pressure<sup>2,3</sup>. The vascular risk associated with hyper-homocysteinemia has been observed to be stronger in hypertensive individuals. More recently, attention has been focused on the direct relations of plasma homocysteine to hypertension. The adverse risk associated with hyper-homocysteinemia appears to have been important bearing in management of these patients. The proposed study is undertaken to observe on the variations in homocysteine concentration in patients of hypertension, hypertension with CAD and hypertension with type 2 DM.

### MATERIALS & METHODS

The present study was undertaken in the Department of Medicine, *MIMS* Medical College & Hospital, Vizianagaram during the period of August 2012 to August 2013. The study included 40 cases of hypertension and age & sex matched 20 healthy control subjects. Patients attending Medicine OPD or admitted to Medicine Ward diagnosed as hypertensive on the basis of JNC-VII criteria were included in the study. Selected cases were subjected to detailed history, thorough clinical

examination supported by necessary laboratory test and imaging studies like ECG, fundoscopy, Echocardiography, Blood sugar, HbA<sub>1c</sub>, Lipid profile, CBC and other routine examinations. Plasma homocysteine was estimated in both case and control groups by CLIA (Chemiluminescence Immune Assay). Patients having hypertensive emergencies, hepatic disease, renal disease, stroke, hypothyroidism, pregnancy and taking any other following drugs like methotrexate, carbamazepine, phenytoin or on any form of vitamin supplementation were excluded from this study.

Plasma homocysteine was estimated using ADVIA Centaur Homocysteine Assay (ADVIA Centaur XP Immunoassay System) which is a one-step competitive immunoassay employing direct chemiluminescence to quantitatively measure total homocysteine in EDTA plasma or serum. Among 60 subjects, 42 (70%) were male and 18 were (30%) were female. In the test group 30 cases (75%) were male and 10 cases (25%) were female. Among 40 cases, majority of cases i.e. 45% cases belong to Group-I (Hypertension), followed by 30% cases belong to Group-II (Hypertension with CAD) and 25% cases belong to Group-III (Hypertension with Type 2 DM) 20 healthy normotensive subjects were taken as control group. Mean systolic blood pressure in cases was 160 mmHg while that of controls was 124 mmHg

Family history was found to be very significant in this study as it was found that 20 patients in test group gave history of hypertension in their first order blood relations. So family history in 50% patients again supports the familial predisposition of the disease. On the contrary only 5 in control group (25%) gave a history of hypertension in their first order relations.

**Table 1: Comparison of Plasma Homocysteine in Different Groups**

Group	No.	Homocysteine μmol/L)Mean±SD	P Value
I- Hypertension	18	36.760± 14.77	< 0.05
II- Hypertension with CAD	12	42.489± 18.99	< 0.001
III-Hypertension ith Type 2 DM	10	40.357± 17.72	< 0.001
<b>Total</b>	<b>40</b>	<b>38.340± 15.250</b>	<b>&lt; 0.001</b>
Control	20	7.360± 1.003	--

The above table shows comparison of plasma homocysteine between control and group-I (hypertension alone), group-II (hypertention with CAD) and group-III (hypertension with Type 2 DM). The variation of plasma homocysteine was more marked in group-II Mean homocysteine level in cases was found to be 38.340 μmol/L while that in controls was 7.360 μmol/L. The range of homocysteine in cases was 21.1 μmol/L to 61.8 μmol/L while that in controls was 6.3 μmol/L to 10.1 μmol/L. The range of plasma homocysteine in male controls was 6.3 μmol/L to 10.1 μmol/L while that in female controls / is 6.4 μmol L to 7.9 μmol/L

**Table 2: Correlation between Homocysteine and Severity of Blood Pressure**

SL. No.	Groups	Homocysteine(μmol/L) Mean±SD	SBP(mmHg) Mean±SD	'r'	p
1	Case	38.340±15.250	160±13.071	0.6741	<0.05
2	Control	7.360±1.003	124±8.233	0.6515	0.05

The above table shows correlation between plasma homocysteine and systolic and diastolic blood pressure which are represented in scatter diagram. Correlation trend line between Homocysteine and systolic Blood pressure:

### Summary

Mean systolic blood pressure is 160.100 ± 13.071 mmHg. Plasma homocysteine value in 3 groups: Group-I (36.760 ± 14.77 μmol/L), Group-II (42.489 ± 18.99 μmol/L) and Group-III (40.357 ± 17.72 μmol/L) reflect greater rise in

hypertension with CAD group (Group-II). Primary objective being study of relationship of plasma homocysteine and hypertension analysis of data (Table 2) shows that mean plasma homocysteine level of  $38.340 \pm 15.250 \mu\text{mol/L}$  when compared with systolic blood pressure  $160.1 \pm 13.071 \text{ mmHg}$  has 'p' value  $< 0.05$  and 'r' value 0.6741. These observation clearly reflects that there is significant relationship between plasma homocysteine and systolic blood pressure

Since plasma homocysteine rise is closely associated with incidence of hypertension, CAD and Type 2 DM and they might have important role in pathogenesis present trend for intervention by homocysteine lowering agents like folic acid, Vit.B-12, Vit.B-6 in addition to control of lipid profile in gaining importance in management of hypertension, CAD and Type 2 DM.

Plasma homocysteine was significantly elevated in hypertensive patients as compared to control. Plasma homocysteine rise is more marked in hypertension with CAD as compared to hypertension with Type 2 DM and hypertension alone. Plasma homocysteine rise is well correlated to systolic blood pressure Plasma homocysteine assay is recommended for all patients of hypertension more so when they are associated with CAD or Type 2 DM.

## REFERENCES

1. Annu Khajuria and Donald S. Induction of monocyte tissue factor expression by homocysteine: a possible mechanism for thrombosis. *Blood*, Vol. 96 No. 3 (August 1), 2000: pp. 966-972
2. Brattstrom L, Wilcken DE. Homocysteine and cardiovascular disease: cause or effect? *Am J Clin Nutr.* 2000; 72: 315–323.
3. Christen WG, Ajani UA, Glynn RJ, Hennekens CH. Blood levels of homocysteine and increased risks of cardiovascular disease: causal or casual? *Arch Intern Med.* 2000; 160: 422–434.
4. Christensen B, Refsum H, Vintermyr O, Ueland PM. Homocysteine export from cells cultured in the presence of physiological or superfluous levels of methionine: methionine loading of nontransformed, transformed, proliferating, and quiescent cells in culture. *J. Cell Biol.* 1991. 146:52–62
5. Clarke, R., Smith, A.D., Jobst, K.A., Refsum, H., Sutton, L. & Ueland, P.M. Folate, vitamin B12, and serum total homocysteine levels in confirmed Alzheimer disease. *Arch. Neurol.* (1998) 55, 1449–1455
6. Desouza C et al. Drugs effecting homocysteine metabolism : impact on cardiovascular risk. *Drugs* 2002; 62 : 605-16.
7. Finkelstein, J.D. Methionine metabolism in mammals. *J. Nutr. Biochem.* (1990) 1, 228–237.
8. Graham IM et al. Plasma homocysteine as a risk factor for vascular disease: the European Concerted Action Project. *JAMA.* 1997; 277: 1775–1781.
9. Harker, L.A., Ross, R., Slichter, S.J. & Scott, C.R. Homocysteine-induced arteriosclerosis: the role of endothelial cell injury and platelet response in its genesis. *J. Clin. Invest.* (1976) 58, 731–741.
10. He J, Tell GS, Tang YC, Mo PS, He GQ. Effect of migration on blood pressure: the Yi People Study. *Epidemiology* 1991. 2:88–97
11. Herbert V, Zalusky R. Interrelation of vitamin B12 and folic acid metabolism: folic acid clearance studies. *J. Clin. Invest.* 1962. 41:1263–76
12. Homocysteine Studies Collaboration. Homocysteine and risk of ischemic heart disease and stroke: a meta-analysis. *JAMA.* 2002; 288: 2015–2022.

13. Jacques PF, Bostom AG, Wilson PW, Rich S, Rosenberg IH, Selhub J. Determinants of plasma total homocysteine concentration in the Framingham Offspring cohort. *Am J Clin Nutr.* 2001; 73: 613–621
14. Jakubowski, H. Translational incorporation of S-nitrosohomocysteine into protein. *J. Biol. Chem.* (2000) 275, 21813–21816
15. Jakubowski, H. Protein homocysteinylation: possible mechanism underlying pathological consequences of elevated homocysteine levels. *FASEB J.* (1999) 13, 2277–2283
16. Kahleova R et al. Essential hypertension in adolescents: association with insulin resistance and with metabolism of homocysteine and vitamins. *Am J Hypertens.* 2002; 15: 857–864
17. Kang SS et al. Hyperhomocysteinemia as a risk factor for occlusive vascular disease. *Ann Rev Nutr,* 1992; 12 : 279-98.
18. Karine Demuth et al. Homocysteine decreases endothelin-1 production by cultured human endothelial cells *Eur. J. Biochem.* (1999) 263, 367-376
19. Kruman II, Kumaravel TS, Lohani A et al. Folic acid deficiency and homocysteine impair DNA repair in hippocampal neurons and sensitized them to amyloid toxicity in experimental models of Alzheimer's diseases. *J Neurosci,* 2002; 22 : 1752-62.