Original Article

CORRELATION OF SERUM HOMOCYSTEINE AND LOW DENSITY LIPOPROTEIN CHOLESTEROL IN HYPERTENSIVE FEMALE PATIENTS

Abdulhalim Salim Serafi[a*]

[a]Department of Physiology, Faculty of Medicine, Umm Al-Qura University (UQU), **Makkah, Saudi Arabia.**
* Corresponding author: asserafi@uqu.edu.sa

Submission Date : 16-09-2019
Revision Date: 06-10-2019
Publication Date: 02-11-2019

Author's Contribution

ASS:Conducted the study and wrote the article.

He is the only author confirmed twice

All authors declare no conflict of interest.

This article may be cited as: Serafi AS. Correlation of serum homocysteine and low density lipoprotein cholesterol in hypertensive female patients. (J Cardiovasc Dis 2019;15(3):59 - 62)

ABSTRACT:
BACKGROUND AND OBJECTIVE: Previous studies suggest that there is a correlation in hyperhomocysteinemia and dyslipidemia which may lead to hypertension and atherosclerosis. However, there is limited data available regarding association of rising levels of homocysteine (Hcy) and lipid abnormalities. Two of the important factors considered to be involved in the pathogenesis of hypertension are homocysteine (Hcy) and (LDL-C) low density lipoprotein cholesterol. However, still there is controversy about the precise role of LDL-C and Hcy in subjects with hypertension. This study was planned to see correlation of homocysteine levels and low density lipoprotein levels in hypertensive females.
MATERIAL AND METHODS: This was case-control observational study, conducted at Physiology Department, Alnoor Specialist Hospital in Makkah, Saudi Arabia over a period of two years from January 2017- January 2019. A total number of 42 female patients were enrolled. The subjects were divided into two groups. One group consisted of 22 hypertensive females (cases) and the other group (control) had 20 normotensive females. The two groups were matched for variables like age and gender. The blood sample of all the patients were collected and sent to pathology lab for determination of Hcy and LDL-C level. The data was analyzed to see the correlation between the plasma Hcy and LDL-C level.
RESULTS:The plot of Hcy against LDL-C showed no significant linear correlation for normal healthy controls (R2: 0.0555; p-value >0.291) but highly significant linear correlation for subjects with hypertension (R2: 0.4366; p-value >0.0015). In hypertensive females group Hcy and LDL-C were having appreciable correlation as compared to control group.
CONCLUSION: Increased Hcy level was positively correlated with LDL-C in hypertensive females.
KEYWORDS: Homocysteine (Hcy), Hypertension, Low Density Lipoprotein Cholesterol (LDL-C), Hcy/LDL-C Association

(J Cardiovasc Dis 2019;15(3):59 - 62)

INTRODUCTION

Hypertension is one of the main contributors in cardiovascular disorders.[1-5] There are variety of factors involved in the pathogenesis of hypertension.[3,4]Two of the important related factors are serum homocysteine (Hcy) and LDL-C. The patients with hypertension show rising trend in serum levels of homocysteine (Hcy)[6-10] as well as LDL-C.[11,12] However, there are studies showing no change in LDL-C in patients with hypertension[13-15] and Hcy in patients with hypertension without carotid plaques.[16] Studies related to interaction and association of Hcy and LDL-C in patients with hypertension showed positive correlation[6,16-19] whereas no correlation was also investigated.[20]

Rising trend of Hcy levels was found in hypertension.[6,8-10] It was also studied that a long-term decrease in LDL cholesterol and blood pressure reduces the life time risk of cardiovascular disorders.[21]Another study revealed a positive correlation between LDL-cholesterol and systolic blood pressure in patients with type 2-diabetes.[11] Another report showed that dietary approaches to stop hypertension (DASH) diet significantly reduced LDL cholesterol.[12] Low or normal and increased levels of LDL-cholesterol were found in two groups of subjects with new onset of arterial hypertension.[13]

However, it was revealed that there is no statistical effect of the modification of LDL-C on association between blood pressure and cardiovascular disorders.[14] Furthermore, a large cohort of patients with hypertension at increased risk of cardiovascular events without previous history of cardiovascular disease other than stroke did not show the influence of LDL-C on cardiovascular events.[15]

The role of Hcy and LDL-C in association revealed that Hcy increases the cardiovascular risk with increased LDL-cholesterol.[17] Prevalence of hyperhomocysteinemia was found associated with higher levels of LDL-C in patients with new-onset hypertension, and LDL-C was considered as an important modifier for changing the concentration of Hcy.[19] Another study found the fasting levels of Hcy and LDL-C were associated with a considerably higher risk of juvenile hypertension.[6]

Patients with essential hypertension having both the TT genotype and the Hcy $\geq$ 10 μmol/L had higher level of hypercholesterolemia and low-density lipoprotein cholesterol suggesting the role of Hcy as an important determinant of the incidence dyslipidemia.[18] Plasma Hcy and LDL-C levels significantly increased in hypertensive patients having carotid plaques than those patients without carotid plaques.[16] Whereas no correlations were found between gene polymorphisms and homocysteine with serum levels of lipid profile in hypertensive patients.[20]

Inspite of all above mentioned studies about the role of Hcy and LDL-C in patients with hypertension of various types, the precise involvement/ association of these factors is not clearly evident in view of controversial data. Hence, this study was conducted to clarify the interactive role of Hcy and LDL-C in subjects with/ without hypertension.

MATERIALS AND METHODS:

This was observational case control study, conducted at Department of Physiology, Alnoor Specialist Hospital in Makkah, Saudi Arabia over a period of two years from January 2017- January 2019. A total number of 42 female patients were enrolled. Patients with diabetes, renal disease, anemia, stroke, hypothyroidism and previous history of myocardial infarction were excluded. The subjects were divided into two groups. One group consisted of 22 hypertensive females (cases = n:22) and the other group (control = n:20) had 20 normotensive females. The two groups were matched for variables like age and gender. Age range was 50-55 years. The blood sample of all the patients were collected and sent to pathology lab for determination of Hcy and LDL-C level. The data was analyzed to see the correlation in the plasma Hcy and LDL-C level.

The Hcy was determined using ELISA kit. Inter-assay variations and intra-assay variations were respectively as < 12% and <10 %. The assay was performed by collecting samples and reagents. The sample was 50 μl with addition of 50 μl of detecting reagent. Incubation was done for one hour at a temperature of 37°C, aspirating and washing three times, addition of 100 μl of detection reagent with incubating half time than the previous and at same temperature, aspirating five times, then adding 90 μl substrate-solution incubating for 20 minutes at 37°C and adding 50 μl stopping solution and then immediately reading was taken at 450 nm. The serum LDL-C was also calculated by using kit methods. Normal Hcy was taken as < 5 μmol/L and LDL-C was labeled as < 100 mg/dl.

The data was entered using MS Excel. Less than 0.05 p-value was considered significant. Statistical tests and analysis was carried out following standard statistical methods.[22] Two-tailed (unpaired t-test) P value, confidence interval, value of t, and F crit, and F were determined and the r2 for linear regression lines was found. Spreadsheets (written

for Excel and workable with Calc program) were helpful for analyzing data. Y intercept, regression coefficient, the r2 value, degree of freedom df, the P value and Y estimator/ X estimator were obtained for comparison purpose.

RESULTS:

The mean ± SEM values of LDL-C (mg/ dl) for normal healthy female controls and female patients with hypertension were respectively as 88.92 ± 2.76 and 110.50 ± 2.24 that indicated extremely statistical significant change (t = 5.9989; df = 40; p value < 0.0001). After adjusting for gender there was significant correlation of Hcy and LDL-C levels in hypertensive females (r = 0.63). However there was no significant correlation of Hcy and LDL-C levels in normotensive females (r = 0.01).

Mean ± SEM values of Hcy (μmol/L) for normal healthy female controls and female patients with hypertension were respectively as 7.92 ±0.37 and 8.93 ±0.45 that indicated not quite statistically significant change (t = 1.7461; df = 40; p value =0.0885).

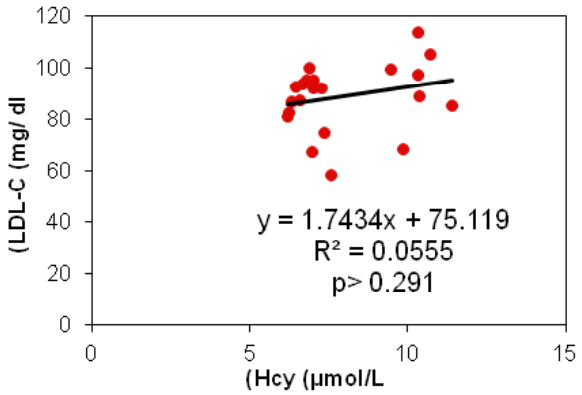

Fig 1: Relationship of serum homocysteine and LDL-cholesterol in normal healthy control females

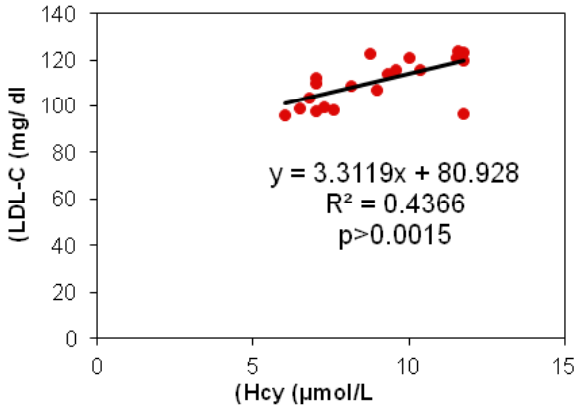

Fig 2: Relationship of serum homocysteine and LDL-cholesterol in female patients with hypertension

Plot of Hcy against LDL-C for normal healthy female controls showed no significant linear correlation (slope: 1.7434; intercept: 75.1191; R2: 0.0555; p-value >0.291). It is shown in Fig. 1.

However, the plot of Hcy against LDL-C for female patients with hypertension showed highly significant linear correlation (slope:3.3119; intercept: 80.9283; R2: 0.4366;P-value >0.0015). It is shown in Fig 2.

DISCUSSION

Findings in the present study are important for understanding the role of serum Hcy and LDL-C in subjects with hypertension and the mechanism of the pathogenesis of hypertension for future studies. Present investigations of level of changes in Hcy and LDL-C in patients with hypertension are similar to several other studies [9,10,12]and are different from others.[13-15]

Quite exciting information in the current report concerns to the comparison for the association of Hcy and LDL-C in female patients with hypertension versus normal healthy female controls. Significant linear correlation among Hcy and LDL-C in female subjects with hypertension is quite similar to findings in other studies,[16,18,19] though no correlation was also documented[20] that contradict the present findings.

Correlation among serum Hcy and LDL-C in patients with hypertension found in current study is quite similar to most of the other studies but varied in the extent of significance in correlation.[6,16-19] Rising trend in Hcy levels occurs in hypertension[6,8,9]and the mechanism whereby Hcy causes hypertension has been explained as due to the effect of Hcy producing imbalance between blood endothelin and nitric oxide concentrations or by increasing calcium ion levels in vascular smooth muscle cells resulting to increase in systolic blood pressure. The predictive nature of Hcy in the development of hypertension was evident in normotensive children of parents with hypertension showing elevated Hcy levels before development of hypertension.[10]

STUDY LIMITATIONS:

The present study presents information for female patients but has no data for male patients having hypertension to be compared with female patients with hypertension. However, the merit of present study is that it is quite well controlled study for comparing the findings in female patients with hypertension against normal healthy age-matched controls.

CONCLUSION:

An increasing level of Hcy has positive correlation with increasing level of LDL-C and may be predisposing cause of hypertension. Decreasing the levels of Hcy may improve dyslipidemia and consequent hypertension. Decreasing the levels of Hcy may improve dyslipidemia and consequent hypertension.

REFERENCES

1.Kearney PM, Whelton M, Reynolds K, Whelton PK, He J. Worldwide prevalence of hypertension: a systematic review. J Hypertens 2004;22(1):11-9.

2.Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J.. Global burden of hypertension: analysis of worldwide data, Lancet2005;365:217–23.

3.Coy V. Genetics of essential hypertensionJ Am Acad Nurse Pract. 2005;17:219–24.

4.Luma GB, Spiotta RT. Hypertension in children and adolescents. Am Fam Physician2006;73:1158–68.

5.Paula Bricarello L, Poltronieri F, Fernandes R, Retondario A, de Moraes Trindade EBS, de Vasconcelos FAG.Effects of the Dietary Approach to Stop Hypertension (DASH) diet on blood pressure, overweight and obesity in adolescents: A systematic review. Clin Nutr ESPEN 2018;28:1-11.

6.Kahleova R, Palyzova D, Zvara K, Zvarova J, Hrach K, Novakova I.Essential hypertension in adolescents:Association with insulin resistance and with metabolism of homocysteine and vitamins. Am J Hypertens 2002;15:857–64.

7.Sun XN, Li YM, Guo H. An approach on correlated factors of genetic polymorphism of the key enzyme in metabolism of homo- cysteine in patients with simple systolic hypertension. Chin Cardiovasc Dis J2003;31:269–73.

8.Yan H, Du JB, Tang CS. The regulatory role of the gasotransmitter hydrogen sulfide upon the aortic structural remodeling in spontaneous hypertensive rats. J Peking Univ2004;36:234–7.

9.Chen L, Ingrid S, Ding Y, Liu Y, Qi JG, Tang CS, et al. Imbalance of endogenous homocysteine and hydrogen sulfide metabolic pathway in essential hypertensive children. Chin Med J2007;120:389–93.

10.Yıldırım A, Keleş F, Özdemir G, Koşger P, Uçar B, Alataş Ö, Kılıç Z.Homocysteine levels in normotensive children of hypertensive parents. Anatol J Cardiol 2015;15(12):1008-13.

11.Nasri H, Yazdani M. The relationship between serum LDL-cholesterol, HDL-cholesterol and systolic blood pressure in patients with type 2 diabetes.Kardiol Pol 2006;64(12):1364-8.

12.Chiu S, Bergeron N, Williams PT, Bray GA, Sutherland B, Krauss RM. Comparison of the DASH (Dietary Approaches to Stop Hypertension) diet and a higher-fat DASH diet on blood pressure and lipids and lipoproteins: a randomized controlled trial. Am J Clin Nutr 2016;103(2):341-7.

13.Cicero AF, Rosticci M, Baronio C, Morbini M, Parini A, Grandi E, D'Addato S, Borghi C; Brisighella Heart Study Group.Eur J Clin Invest 2014;44(10):926-32.

14.Tsukinoki R, Okamura T, Watanabe M, Kokubo Y, Higashiyama A, Nishimura K, Takegami M, Murakami Y, Okayama A, Miyamoto Y. Am J Hypertens 2014;27(11):1362-9.

15.Nguyen LS, Procopi N, Salem JE, Squara P, Funck-Brentano C.Relation between baseline LDL-cholesterol and cardiovascular outcomes in high cardiovascular risk hypertensive patients: A post-hoc SPRINT data analysis.Int J Cardiol 2019;286:159-161

16.Zhao X, Bo L, Zhao H, Li L, Zhou Y, Wang H.Descriptive study of the relationship between the subclinical carotid disease and biomarkers, carotid femoral pulse wave velocity in patients with hypertension. Clin Exp Hypertens 2018;40(3):274-280.

17.Daly C, Fitzgerald AP, O'Callaghan P, Collins P, Cooney MT, Graham IM; COMAC Group. Homocysteine increases the risk associated with hyperlipidaemia.Eur J Cardiovasc Prev Rehabil 2009;16(2):150-5.

18.Liu Y, Li K, Venners SA, Hsu YH, Jiang S, Weinstock J, Wang B, Tang G, Xu X. Individual and Joint Associations of Methylenetetrahydrofolate Reductase C677T Genotype and Plasma Homocysteine With Dyslipidemia in a Chinese Population With Hypertension. Clin Appl Thromb Hemost 2017;23(3):287-293.

19.Wang W, Ji P, Wang Y, Guo H, Bian R, Xu J, Xiong Y. Prevalence of hyperhomocysteinemia and its associated factors in patients with primary hypertension in Chinese urban communities: A cross-sectional study from Nanjing. Clin Exp Hypertens 2018;40(5):495-500.

20.Li WX, Lv WW, Dai SX, Pan ML, Huang JF. Joint associations of folate, homocysteine and MTHFR, MTR and MTRR gene polymorphisms with dyslipidemia in a Chinese hypertensive population: a cross-sectional study. Lipids Health Dis 2015;14:101.

21.Václavík J.News in the treatment of hypertension and dyslipidemia. Vnitr Lek 2017;63(5):333-337.

22. Zahir H, Javaid A, Rehman R, Hussain Z. Statistical concepts in biology and health sciences. J Ayub Med Coll Abbottabad 2014;26(1):95-7.