

## THE EVALUATION OF RELATIONSHIP BETWEEN CIRCULATING HOMOCYSTEINE AND SYSTOLIC BLOOD PRESSURE (SBP): A CROSS-SECTIONAL STUDY

Dr. Shreya Nigoskar<sup>1</sup>, Dr. Naresh Kumar<sup>2\*</sup>

1. Professor, 2. Research Scholar, Department of Biochemistry, Index Medical College, Hospital and Research center, Malwanchal University, Indore (M.P.)

\*Corresponding author – Dr. Naresh Kumar

Email id – [drnareshkk@gmail.com](mailto:drnareshkk@gmail.com)

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### ABSTRACT

**Background:** There is an increase in the prevalence of diseases such as stroke, cardiovascular diseases, hypertension, diabetes, and cancer, non-communicable diseases are now projected as a global health crisis. Among the non-communicable diseases, hypertension claims a number of first because of the following reasons; the most common chronic condition, a major risk factor for heart disease and stroke, accounts for the most drug prescriptions, and throughout the world, it is the number one attributable risk for deaths. **Material & Methods:** The present cross-sectional case-control study was conducted at the Department of Biochemistry at index hospital Indore. The study duration was April 2019 and March 2020. A sample size of 150 was calculated at a 90 % confidence interval at a 5 % acceptable margin of error. Clearance from Institutional Ethics Committee was taken before the start of the study. Written informed consent was taken from each study participant. Results: The age of the subjects in the study group ranged from 20 to 50 years. The mean and standard deviation for the age of the Cases and control individuals were  $27.81 \pm 6.1$  and  $26.92 \pm 5.6$  respectively, there was no significant difference among the cases and controls with reference to the age. The significant difference is there in BMI, WHR, Homocysteine level, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Pulse Pressure, Heart rate (Mean and SD) between cases and control. **Conclusion:** In our study, we concluded that the hypertensive patients have high homocysteine levels compared to the control. Blood total homocysteine is a strong, independent risk factor for CVD, the relationship between elevated homocysteine and CVD is causal

**Keywords:** Diastolic Blood Pressure, Mean Arterial Pressure, Pulse Pressure, Heart rate.



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### INTRODUCTION

“The greatest wealth is health;” nowadays, in the modernized and computerized world to become wealthier is easy but to become healthier is a big task. In the past, the world has faced challenges as complex as those now ascribed by a trio of threats: First, the undernutrition and the unfinished agenda of infections; second, the increasing global burden of non-communicable diseases; and third the

complications arising from globalization itself, like the ill effects of climate change.<sup>1</sup>

Before the antibiotic era, communicable diseases had their dominant role but with the advent of new efficient antibiotics, communicable diseases are now no more a big problem. Since there is an increase in the prevalence of diseases such as stroke, cardiovascular diseases, hypertension, diabetes, and

cancer, non-communicable diseases are now projected as a global health crisis.<sup>2</sup> The world health organization's global status report<sup>3</sup> (2010) states that non-communicable diseases are the leading cause of worldwide deaths contributing to 60%. In India, the situation is very grim. In 2005, total mortality of 53% and 44% of daily adjusted life years lost was attributed to non-communicable diseases.

By 2030, the total mortality by non-communicable diseases would be 67% in India.<sup>3</sup> The alarming rise in the magnitude of non-communicable diseases demands urgent attention.<sup>3</sup> Recently, the world health organization identified six risk factors<sup>4</sup> within the non-communicable diseases for deaths.

The six risk factors<sup>4</sup> are hypertension; impaired glucose tolerance; tobacco usage; dyslipidemia; lack of physical activity and obesity. Of the above-said risk factors, hypertension is responsible for 13% of total deaths in the world followed by tobacco usage (9%); impaired glucose tolerance (6%); physical inactivity (6%), and obesity (5%). Among the non-communicable diseases, hypertension claims a number of first because of the following reasons; the most common chronic condition, a major risk factor for heart disease and stroke, accounts for the most drug prescriptions, and throughout the world, it is the number one attributable risk for deaths.<sup>5</sup>

An elevated plasma homocysteine level is an established independent risk factor for cardiovascular disease.<sup>5,6</sup> Moreover, a higher plasma homocysteine level has been linked with higher blood pressure.<sup>7,8</sup> Dietary intake of vitamins B6, B12, and folic acid have been reported to decrease the plasma homocysteine level<sup>9</sup>. These vitamins may influence BP by mediating the effects on the homocysteine level.

Meanwhile, folic acid has been reported to enhance endothelial nitric oxide synthase and to have beneficial effects on endothelial function, largely independently of homocysteine decrease.<sup>10</sup> It is also possible that folic acid can directly affect the blood pressure level. Indeed, some studies have demonstrated that higher folic acid intake is associated with a lower or decreased risk of incident hypertension among adults<sup>11</sup>

This study is planned to find out the association of Homocysteine in hypertensive patients in the Indian population.

## MATERIAL & METHODS

The present cross-sectional case-control study was conducted at the Department of Biochemistry at index hospital Indore. The study duration was April 2019 and March 2020. A sample size of 75 was calculated at a 95 % confidence interval at 11.32% acceptable margin of error by epi info software version 7.2.

Patients were enrolled from the outpatient department and ward by simple random sampling. Clearance from Institutional Ethics Committee was taken before the start of the study. Written informed consent was taken from each study participant.

All the volunteering individuals with hypertension without medication and aged between 20-60 years of both male & female genders were included in the study design. In the present study patient below 20 and above 60 years, Patients with medications, pregnant women, or any Terminal Illness (Cancer, HIV, etc) were excluded.

The demographic details and clinical history, including the history of recent MI, stroke with residual paresis, uncontrolled CHF, a peripheral arterial disease with evidence of tissue injury or loss, TIAs were recorded for each study participant.

Waist circumference, Waist-hip ratio, BMI, homocysteine levels, Blood pressure, and other Clinical data of all patients were collected and analyzed. Sample collection: After overnight fasting for 8 – 12 hrs, approx. 3ml blood sample for Homocysteine in the red top plane tube. Samples will be centrifuged at 3000rpm for 10 min for serum separation. Homocysteine was analyzed by direct chemiluminometric technology on Cobas E411 CLIA.

**Statistical analysis:** Student t-test will be used along with other appropriate statistical analyses. p-Value  $\leq 0.05$  will be considered as significant. Data will be entered on an excel sheet and SPSS 18 software shall be used.

## RESULTS

In the present study, 150 study participants of age between 20-60 years of both male & female genders were enrolled. The mean age of these elderly patients was 27.26years.

**Table 1 - Cases showing raised homocysteine**

S. homocysteine	Frequency	Percentage
Abnormal	56	74.7
Normal	19	25.3
<b>Total</b>	<b>75</b>	<b>100.0</b>

The above table shows that out of cases a maximum of 74.7% were having abnormal levels of serum Homocysteine, whereas 25.3% were having normal levels of serum Homocysteine.

**Table 2 Comparison between hypertensive patients(cases) and controls.**

Parameter	Cases		Control	P-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Age	27.81 ± 6.1	26.92 ± 5.6	26.92 ± 5.6	0.350967
BMI	28.52 ± 3.19	23.1 ± 1.66	23.1 ± 1.66	<0.0001
WHR	0.88 ± 0.04	0.77 ± 0.04	0.77 ± 0.04	0.0068**
Homocysteine (µM/L)	18.74 ± 1.79	11.03 ± 1.87	11.03 ± 1.87	<0.0001*
Systolic Blood Pressure	145.21 ± 17.9	108.21 ± 8.9	108.21 ± 8.9	<0.0001
Diastolic Blood Pressure	98.51 ± 8.8	82.21 ± 5.2	82.21 ± 5.2	<0.0001
Mean Arterial Pressure	85.2 ± 7.6	75.9 ± 4.8	75.9 ± 4.8	<0.0001
Pulse Pressure	49.8 ± 5.8	38.8 ± 3.4	38.8 ± 3.4	<0.0001
Heart rate	92 ± 8.1	74 ± 9.2	74 ± 9.2	<0.0001

## DISCUSSION

Hypertension affects 20% of the adult population worldwide and is considered to be a multifactorial disorder of unknown etiologies.<sup>12</sup> If a major cardiovascular risk factor such as hypertension is controlled it may reduce the cardiovascular disease burden for the region. Although hypertension has a high prevalence rate, it

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has been acknowledged as one of the modifiable risk factors for cardiovascular disease associated with stroke, heart disease, and end-stage kidney disease.<sup>13</sup>

Since individuals with hypertension have a higher predisposition for cardiovascular disease, premature death may occur in individuals whose BP

is poorly controlled.<sup>14</sup> The use of non-pharmacological methods has been shown to have the ability to substantially reduce BP in adults with hypertension.<sup>13</sup> The two most recognized non-pharmacological methods used to manage and control BP in adults are Increased participation in physical activity and the adoption of a healthy diet.<sup>15</sup>

We found that systolic blood pressure was  $145.21 \pm 17.9$  in hypertensives as compared to  $108.21 \pm 8.9$  in normotensives and diastolic blood pressure was  $98.51 \pm 8.8$  in hypertensives as compared to  $82.21 \pm 5.2$  in normotensives. Homocysteine levels were high hypertensives group and statically significant. The result of Hongxu Wu et al accordance with our study found Serum total Homocysteine concentrations were positively associated with both SBP and DBP levels in a general Chinese adult population.<sup>16</sup> Hyperhomocystenimia belongs among the congenital hypercoagulable states & is a long known vascular disease risk factor. Hyperhomocysteinemia has been suggested as a possible risk factor in women suffering from recurrent abortions, eclampsia, pre-eclampsia, placental abruption, IUGR, NTD's, thromboembolic events, etc.

A meta-analysis of 72 studies has validated that circulating blood total homocysteine can predict the different cardiac diseases like ischemic heart disease, pulmonary embolism, DVT, and stroke.<sup>5</sup> the authors also revealed by the results of the meta-analysis make an available further strong proof for an underlying association between raised blood homocysteine and cardiac vascular disease. The authors evaluate that lowering blood total homocysteine by  $3\mu\text{mol/L}$  would decrease a person's threat of deep vein thrombosis by 25 %, ischemic heart disease by 16 %, and stroke by 24 %. A further suggestion for the outcome of homocysteine decline on CVD risk comes from a great epidemiologic study of the effect of the folate fortification program in the USA and Canada.<sup>17</sup>

The fortification program was initiated in 1996 as an effort to check birth defects, but the study found the program also reduced the mortality rate from stroke and heart attacks. For example, stroke mortality declined almost 5 % per year following fortification compared with a decline of only 1 % before 1997. Overall, the researchers assess the folate fortification program prevented 31,000 deaths from stroke and 17,000 deaths from heart disease every year from 1998 to 2001.<sup>17</sup> Patients with apparent CVD or at

high risk of developing CVD should have their total homocysteine measured and be encouraged to adhere to their physician's advice for treatment if the level is  $>15\mu\text{mol/L}$ . Total homocysteine levels can be lowered by various homocysteine-lowering agents, such as vitamin supplements, betaine, and N-acetylcysteine.<sup>18</sup> Lifestyle changes can also help reduce levels and the adoption of healthy behavior's, such as a balanced diet, cessation of smoking, regular exercise, and consumption of only moderate amounts of caffeine and alcohol, all have considerable positive health benefits beyond the prevention of CVD.

## CONCLUSION

In our study, we concluded that the hypertensive patients have high homocysteine levels compared to control. The potential interaction between these in relation to blood pressure should also be examined in future studies. Blood total homocysteine is a strong, independent risk factor for CVD, the relationship between elevated homocysteine and CVD is causal and probably due to multiple, potentially synergistic, pathogenetic mechanisms. The modest reduction in blood total homocysteine is predicted to confer large reductions in risk from CVD  $<15\mu\text{mol/L}$  is considered a normal fasting level of blood total homocysteine, although European laboratories tend to use a value of  $12\mu\text{mol/L}$  as the upper reference limit in adults Upper reference limits depend on age and whether an individual has access to food fortified with folate or dietary supplements. Measurement of blood total homocysteine is suggested for risk assessment in CVD patients, diagnosis of the rare genetic disease homocystinuria, and identification of individuals with (or at risk from) folate or cobalamin deficiency.

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