

SERUM HOMOCYSTEINE;

Hypertensive Patients

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ABSTRACT.....objective: To evaluate the serum homocysteine level in patients with hypertension at Liaquat University Hospital Hyderabad. **Patients and methods:** This six months study was conducted at Liaquat University Hospital Hyderabad. All the hypertensive patients **FOR \geq YEARS DURATION OF \geq YEARS OF AGE AND EITHER GENDER VISITED AT THE CARDIAC LOGY OPD OR ADMITTED IN CARDIAC WARD WERE REGISTERED AND EVALUATED FOR THEIR HOMOCYSTEINE LEVEL THE NORMAL PLASMA HOMOCYSTEINE LEVEL IS BETWEEN TO μ MOL L THE RESULTS OF PLASMA HOMOCYSTEINE LEVEL WERE INTERPRETED AS NORMAL MODERATE INTERMEDIATE AND SEVERE ACCORDING TO THE REFERENCE RANGE MODERATE TO μ MOL L INTERMEDIATE TO μ MOL L SEVERE μ MOL L THE FREQUENCY AND PERCENTAGE WAS CALCULATED** for hyperhomocysteinemia in hypertensive patients. The chi-square and independent t-test was applied between categorical variables at 95% confidence interval and the p-value \leq 0.05 was considered as statistically significant. **Results:** Total 120 hypertensive patients were registered for study. Of these 86(71.7%) were males and 34 (28.3%) were female. Regarding plasma homocysteine level, hyperhomocysteinemia was observed in 99(83%) hypertensive patients, of which 75(75.8%) were males and 24(24.2%) were females while the 21(17.5%) subjects had normohomocysteinemia [$p=0.04$]. According to the categorical classification of plasma homocysteine level, the moderate was identified in 58(48%), intermediate in 19 (16%) and severe in 22 (18%) [$p = 0.04$]. The mean systolic and diastolic blood pressure in overall population was 160 ± 26 and 90 ± 16 [$p=0.02$] respectively. The mean \pm SD for plasma homocysteine level in overall population was 72.83 ± 12.61 whereas the mean \pm SD of patients with normal, moderate, intermediate and severe plasma homocysteine level was 7.1 ± 1.8 , 21 ± 2.7 , 60 ± 12.4 and 116 ± 7.3 respectively. **Conclusion:** It is observed that serum homocysteine appears to be raised in patients with hypertension. The hyperhomocysteinemia may be involved in the induction and sustaining of

Key words: Hypertension, Homocysteine.

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INTRODUCTION

Hypertension is defined as a mean systolic blood pressure above 140 mm Hg and a mean diastolic blood pressure above 90 mm Hg. Estimates suggested that approximately 972 million (26.4%) adults around the globe had hypertension in the year 2000¹. These numbers are expected to approach 1.56 billion (29.2%) by the year 2025, a 60% rise in the total number of people affected. Due to a higher growth rate, lower socioeconomic status and presence of a greater array of risk factors, developing nations will constitute the bulk of this increase². Hypertension in Pakistan remains a major health problem; with a prevalence of 17.9% in the adult population, there are an estimated 10 million hypertensives³. The effects of hypertension on cardiovascular and renal mortality and morbidity are well-established worldwide³. The National Health Survey 1990-94 of Pakistan reported 17.9%

prevalence of hypertension among adults 15 years and above, with substantially higher prevalence in urban areas⁵ (i.e. Urban 21.5% and Rural 16.2%). The community-based prevalence of hypertension in this study was 26%⁴. The prevalence of stage 1 and 2 hypertension was more common and according to Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, stage 1 and 2 hypertension responds well to non-pharmacological interventions, such as weight reduction, exercise etc. In ideal circumstances, it can be assumed that knowledge of hypertension may lead to better outcome for hypertensive subjects, as they may take steps to control their blood pressure with appropriate medical care and lifestyle modifications⁴.

The Homocysteine (Hcy) is an amino acid, is a homologue of the amino acid cysteine, differing by an

additional methylene (-CH₂-) group⁵. It is biosynthesized from methionine by the removal of its terminal methyl group and can be recycled into methionine or converted into cysteine with the aid of B-vitamins⁶. Increased circulating levels of homocysteine are seen in with homocysteinuria, patients with homozygosity for the thermolabile variant of methylenetetrahydrofolate reductase, or individuals with dietary deficiency of folate and or cyanocobalamin⁷. Increase in plasma concentration of homocysteine is common in patients with stroke, peripheral vascular disease and coronary disease and confer an independent risk of atherosclerosis⁸. Several epidemiologic studies have demonstrated that elevated plasma total homocysteine has a modest effect on the risk of cardiovascular disease⁹. The vascular risk associated with hyperhomocysteinemia has been observed to be stronger in hypertensive individuals¹⁰. More recently, attention has been focused on the direct relations of plasma homocysteine to blood pressure and hypertension because of the suggestion that the adverse risk associated with hyperhomocysteinemia might be mediated in part by the positive association of homocysteine with hypertension¹¹.

Therefore the present study was conducted at tertiary care teaching hospital of Hyderabad which evaluates the serum homocysteine levels in patients with hypertension. The early identification and treatment of hyperhomocysteinemia can save the patient to acquire life threatening complications of coronary vascular disease.

PATIENTS AND METHODS

This six months study, from October 2011 to March 2012 was conducted at Liaquat University Hospital Hyderabad. All the hypertensive patients for ≥ 01 years duration, of ≥ 35 years age and either gender visited at the cardiology OPD or admitted in cardiac ward were registered and evaluated for their homocysteine level. A written consent was taken from all patients for

participation in the study after explaining the full procedure in relation to the study. The hypertension was categorized as stage 1 and stage 2 according to the JNC-7¹². **THE NORMAL PLASMA HOMOCYSTEINE LEVEL IS BETWEEN TO $\mu\text{MOL L}$ THE RESULTS OF PLASMA HOMOCYSTEINE LEVEL WERE INTERPRETED AS NORMAL MODERATE INTERMEDIATE AND SEVERE ACCORDING TO THE REFERENCE RANGE MODERATE TO $\mu\text{MOL L}$ INTERMEDIATE TO $\mu\text{MOL L}$ SEVERE $\geq \mu\text{MOL L}$**

THE EXCLUSION CRITERIA OF THE STUDY WERE THE PATIENTS ALREADY ON FOLIC acid, pyridoxine and vitamin B12 therapy and who refused to give written consent for participation in the study. All the maneuvers were performed by the cooperation of whole research team and were under the medical ethics. The data was collected on pre-designed proforma and then entered, saved and analysis in SPSS version. 10. The frequency and percentage was calculated for hyperhomocysteinemia in hypertensive patients. The frequency and percentage was also calculated from gender distribution and stages of hypertension. The mean \pm SD was calculated for quantitative variables. The chi-square and independent t-test was applied between categorical variables at 95% confidence interval and the p-value ≤ 0.05 was considered as statistically significant.

RESULTS

During six month study period total 120 hypertensive patients were registered for study. Of these 86(71.7%) were males and 34 (28.3%) were female. The mean age \pm SD for male and female was 52.86 ± 9.74 and 55.72 ± 7.93 respectively. The distribution of hypertension, frequency of hyperhomocysteinemia in relation to gender and severity is shown in Table.I, II and III where as the hypertension in relation to severity of hyperhomocysteinemia is shown in Table.IV. The mean systolic and diastolic blood pressure in overall population was 160 ± 26 and 90 ± 16 [p=0.02]

respectively. The mean systolic and diastolic blood pressure in hyperhomocysteinemic patients was 170 ± 8.75 and 105 ± 12.84 whereas the mean systolic and diastolic blood pressure in

normohomocysteinemic subjects was 125 ± 7.43 and 85 ± 9.72 . The mean \pm SD for plasma homocysteine level in overall population was 72.83 ± 12.61 whereas the mean \pm SD of patients with normal, moderate,

| HYPERTENSION | | | | |
|--------------|------------|------------|------------|---------|
| Gender | Stage 1 | Stage 2 | Total | p-value |
| Male | 45 (80.4%) | 41 (64.1%) | 86 (71.7%) | 0.048 |
| Female | 11 (19.6%) | 23 (35.9%) | 34 (28.3%) | |
| Total | 56 (100%) | 64 (100%) | 120 (100%) | |

Table-I. Gender distribution in relation to stage of hypertension

*P-value is statistically significant, Pearson Chi-square value = 3.90; df = 1

| HOMOCYSTEINE | | | | |
|--------------|------------|------------|------------|---------|
| Hypertension | Raised | Normal | Total | p-value |
| Male | 75 (75.8%) | 11 (52.4%) | 86 (71.7%) | 0.03* |
| Female | 24 (24.2%) | 10 (47.6%) | 34 (28.3%) | |
| Total | 99 (100%) | 21 (100%) | 120 (100%) | |

Table-II. Frequency of hyperhomocysteinemia in hypertension

*P-value is statistically significant, Pearson Chi-square value = 4.66; df = 1

| HYPERTENSION | | | | |
|--------------|------------|------------|------------|---------|
| Homocysteine | Male | Female | Total | p-value |
| Normal | 13 (15.1%) | 08 (23.5%) | 21 (17.5%) | 0.04* |
| Moderate | 48 (55.8%) | 10 (29.4%) | 58 (48.3%) | |
| Intermediate | 10 (11.6%) | 09 (26.5%) | 19 (15.8%) | |
| Severe | 15 (17.4%) | 07 (20.6%) | 22 (18.3%) | |
| Total | 86 (100%) | 34 (100%) | 120 (100%) | |

Table-III. Severity of hyperhomocysteinemia in relation to gender

*P-value is statistically significant, Pearson Chi-square value = 8.02; df = 3

| HYPERTENSION | | | | |
|--------------|------------|------------|------------|---------|
| Homocysteine | Stage 1 | Stage 2 | Total | p-value |
| Normal | 16 (28.6%) | 05 (7.8%) | 21 (17.5%) | 0.02* |
| Moderate | 25 (44.6%) | 33 (51.6%) | 58 (48.3%) | |
| Intermediate | 06 (10.7%) | 13 (20.3%) | 19 (15.8%) | |
| Severe | 09 (16.1%) | 13 (20.3%) | 22 (18.3%) | |
| Total | 56 (100%) | 64 (100%) | 120 (100%) | |

Table-IV. The hypertension in relation to severity of hyperhomocysteinemia

*P-value is statistically significant, Pearson Chi-square value = 9.68; df = 3

intermediate and severe plasma homocysteine level was 7.1 ± 1.8 , 21 ± 2.7 , 60 ± 12.4 and 116 ± 7.3 respectively.

DISCUSSION

Hypertension is a common, chronic condition and most cases have an unclear etiology¹³. In cross-sectional studies, higher plasma homocysteine levels are associated with higher levels of systolic blood pressure (SBP) and diastolic blood pressure (DBP)^{14,15}.

The results of our study confirm that plasma homocysteine is largely independent of smoking or body mass index but it may be related to hypertension as 99 out of 120 subjects in the present study showed an increased level of plasma homocysteine. The findings here in are consistent with past reports that, although limited for various reasons, considered the relation of homocysteine to blood pressure¹⁶. Araki, et al¹⁶ reported that average homocysteine levels were higher in hypertensive compared with normotensive subjects. Sutton-Tyrrell, et al¹⁷ found an increased risk of isolated systolic hypertension in the elderly among those with higher homocysteine. Neither study^{16,17} provided a quantitative estimate of the strength of the association of homocysteine with blood pressure throughout its continuous range. Drzewoski et al reported in their studies that elevated blood levels of homocysteine is strongly related to an increased risk for atherosclerosis and cardiovascular disease¹⁸.

Hyperhomocysteinemia has been suggested to evoke hypertension due to its role in endothelial dysfunction¹⁹. Possible mechanisms involve increased oxidative injury to the endothelium, proliferation of vascular smooth muscle cells, and inhibition and degrading of arterial structural components such as collagen, elastin, and proteoglycans¹⁹. In addition, high levels of homocysteine possibly decrease bioavailability of nitric oxide also termed endothelium-derived relaxing factor and thereby impair vasodilatation²⁰. Indeed,

higher homocysteine concentrations are associated with more advanced systemic arterial stiffness and greater blood pressure response to stress in hypertensive patients and healthy volunteers^{21,22}. In present study the male population was predominant to have hyperhomocysteinemia the finding is consistent with the study by Fowdar, et al²³. In current series the hyperhomocysteinemia was more likely in stage 2 hypertension and the finding is also observed in former literature by Al-Baldawi At²⁴.

This study found an independent association of homocysteine with blood pressure. Serum homocysteine levels were positively associated with hypertension. The homocysteine-blood pressure association should be investigated further in an extensive and advance multidisciplinary manner at various health centers.

CONCLUSION

It is observed that serum homocysteine appears to be raised in patients with hypertension. The hyperhomocysteinemia may be involved in the induction and sustaining of hypertension. Therefore, more advance studies and clinical trials focused on plasma homocysteine and blood pressure will improve our understanding of these associations with the goal of reducing the public health burden of hypertension.

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What you are is God's gift to you;
what you make of yourself is your gift to God.

Jewish Proverb