

SERUM HOMOCYSTEINE CONCENTRATIONS IN PATIENTS WITH HYPERTENSION

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Background: Elevated plasma homocysteine is a known risk factor for atherosclerotic vascular disease. In fact, it is an independent risk factor similar to smoking or hyperlipidemia but it is under recognized among the doctors of Pakistan. An elevated homocysteine level induces thrombogenicity, causes procoagulant state and promotes the proliferation of smooth muscle cells. This study was carried out to find out the serum homocysteine levels in patients with known hypertension. **Methods:** One hundred patients more than 60 years of age of both the sexes with documented hypertension were selected from medical wards and cardiology ward of Civil Hospital Karachi. Study subjects had no history of atherosclerotic disease or diabetes mellitus. Homocysteine estimation was done by FPIA method on IMX. **Results:** It was seen that 80% patients selected had an elevated homocysteine levels (18.77 ± 1.9 as against 5–15 taken as normal). **Conclusion:** We have observed that serum homocysteine is raised in most of the patients with hypertension.

Keyword: Homocysteine, Hypertension, Blood Pressure

INTRODUCTION

Homocysteine is a curious sulphur containing amino acid formed during methionine metabolism.¹ It can dimerise to homocysteine, or form disulphide bonds with proteins to form so-called 'protein-bound' homocysteine. In plasma 80% of homocysteine is protein bound.² Homocysteine is a four-carbon amino acid [$\text{HS}(\text{CH}_2)_2\text{CHNH}_2\text{COOH}$], resulting from the demethylation of methionine. Homocysteine is a dimer composed of two oxidized molecules of homocysteine linked by a disulfide bond. Multiple forms of homocysteine circulate in blood: the majority (65%) is disulfide linked to protein; ~30% is in an oxidized state, mostly as disulfide links to itself or cysteine; and ~1.5–4% is free reduced form. Storage of plasma or serum causes redistribution of these forms with an increase in the protein-bound fraction.³ Increase in plasma concentration of homocysteine is common in patients with stroke, peripheral vascular disease,⁴ and coronary disease⁵ and confer an independent risk of atherosclerosis.⁶

Measurement of total plasma or serum homocysteine represents the sum of oxidized and protein bound homocysteine. Homocysteine contains a reactive sulfhydryl group that can react with plasma constituents and this may promote oxidative damage. An elevated homocysteine level therefore induces thrombogenicity, causes procoagulant state and promotes the proliferation of smooth muscle cells.⁷

This study was carried out to find out the serum homocysteine levels in patients with known hypertension.

SUBJECT AND METHOD

The study was carried out in the medical and cardiology ward of Civil Hospital Karachi in collaboration of Abbott Laboratories Pakistan. 100 subjects with known hypertension were taken.

We defined hypertension as systolic blood pressure more than 140 mm Hg or diastolic blood pressure more than 90 mm Hg or current use of antihypertensive medications.

The data collection was standardized through the use of similar methodology, protocol and procedure using a standard questionnaire. The questionnaire provided information about type of work, smoking history, medical and family history of cardiovascular disease and hypertension. Weight was measured on a balance scale while height was measured in the standing position. Blood pressure of subject was measured twice in the right arm after 5 minutes of rest, using a standard mercury sphygmomanometer. Values from the second measurement were used in this study.

The subjects were asked to fast for 10 hours. After all aseptic measures 6 ml of blood was collected from the antecubital vein while the subjects were sitting up right. Strictly predefined protocol was used for specimen preparation. Blood was collected in a gel barrier silicon coated neotube from Nipro Japan. The additive free blood tubes were put immediately on ice in an icebox. Whole blood tubes were kept at room temperature until clotting was complete. Those samples that showed sign of haemolysis were discarded. Samples were centrifuged at 1000 rpm for 10 minutes within one hour of collection; serum was separated and stored in aliquots in deep freezer at -20°C until assayed.

Samples were analyzed in one run at the end of the study to omit between run serum analytical variations. Serum homocysteine was analyzed by FPIA (Fluorescence Polarization Immunoassay) using the IMX analyzer of Abbott Laboratories Pakistan. Levels between 5 and 15 micromoles per litre ($\mu\text{mol/L}$) are considered normal

RESULTS

A total of 100 subjects were studied. The results are summarized in Tables 1–2. Table-1 shows the mean values of age, weight, height and body mass index of the subjects. Table-2 shows the mean value of blood pressures and mean values of the serum homocysteine levels. It was observed that 80 out of the 100 subjects had elevated homocysteine level.

Table-1: Age, Weight, height, BMI (n=100)
(The values are expressed as Mean \pm SEM)

Male: Female	60:40
Age (years)	44.86 \pm 1.15
Weight (kg)	60.54 \pm 2.26
Height (m)	1.57 \pm 0.07
BMI (kg/m^2)	23.81 \pm 1.25

BMI: body mass index

Table-2: Systolic blood pressure, Diastolic blood pressure and Homocysteine (n=100)
(The values are expressed as Mean \pm SEM)

SBP (mmHg)	150.25 \pm 3.35
DBP (mmHg)	104.75 \pm 2.76
Homocysteine ($\mu\text{mol/l}$)	18.77 \pm 1.9

SBP: systolic blood pressure, DBP: diastolic blood pressure

DISCUSSION

Elevated blood pressure is a significant strong and independent risk factor for coronary artery disease both in men and women.⁸ Conventionally increase in blood pressure more than the normal is called as hypertension. There is no dividing line between normal and high blood pressure. WHO and Framingham studies use 160/95 mm Hg as hypertension.⁹ In 1969, McCully¹⁰ recognized that an elevation in the concentration of plasma homocysteine can lead to an increased risk of cardiovascular disease. The results of our screening survey reconfirm that plasma homocysteine is largely independent of smoking or body mass index but it may be related to hypertension as 80 out 100 subjects in the present study showed an increased level of plasma homocysteine.

Drzewoski *et al* reported in their studies that elevated blood levels of homocysteine is strongly related to an increased risk for atherosclerosis and cardiovascular disease.¹¹ In 1995 meta analysis of 27 observational studies involving a total of approximately 4000 participants, it was reported that hyperhomocysteinemia, defined as plasma homocysteine level above 90th or 95th percentile of level in control, was associated with an increased risk of fatal and non fatal atherosclerotic vascular disease in the coronary and cerebral circulation.

In conclusion, we have observed that serum homocysteine appears to be raised in patients with hypertension. This study was limited and this topic needs to be further worked upon.

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