# THE EFFECT OF ESSENTIAL HYPERTENSION ON SERUM URIC ACID LEVEL

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*Patient with arterial hypertension and no definable cause are said to have essential, primary or idiopathic hypertension. A total of 100 patients suffering from essential hypertension and 100 control subjects with almost same mean age and sex distribution were enrolled in this study. Levels of serum uric acid, total cholesterol, TG, and HDL-c were determined by enzymatic colorimetric method. Serum LDL-c and VLDL-c was calculated by using Friedewald and Wilson's formulae. The study was aimed to find out the levels of serum uric acid and lipid profile in patients with essential hypertension and to compare them with levels of normal healthy individuals. Results show increased level of serum uric acid and lipid parameters except for HDL-c, which was significantly, decreased in patients with essential hypertension as compared to the control subjects. Variations in aforementioned parameters were also observed on comparing the obese and the non-obese patients. It can be concluded from the present study that the essential hypertension is associated with abnormalities in the levels of serum uric acid and lipid profile.*

## INTRODUCTION

Hypertension is a sustained elevation of systemic arterial pressure[1]. Elevated blood pressure is defined as systolic blood pressure $\geq$ 140mm Hg and/or diastolic blood pressure $\geq$ 90 mmHg[2]. In the primary (essential) hypertension no cause can be established. About 95% of cases fall in the category of essential hypertension. Pathogenesis of essential hypertension is multi-factorial. Genetic factors play an important role. Other factors that may be involved in the pathogenesis of essential hypertension are sympathetic nervous system hyperactivity, defect in natriuresis, elevated levels of intracellular $Na^+$ and $Ca^{+2}$, and high plasma rennin activity which can account for approximately 10% of essential hypertension. Exacerbating factors include obesity, high sodium intake, and excessive use of alcohol, cigarette smoking, lack of exercise, stress, polycythaemia, non steroidal anti-inflammatory drugs (NSAIDs) and low potassium intake. In secondary hypertension a specific cause of hypertension can be found. Secondary causes include oestrogens use, renal diseases, renal vascular hypertension, primary hyper-aldosteronism, Cushing's syndrome, pheochromocytoma, coarctation of aorta, hypertension associated with pregnancy, acromegaly, hyperthyroidism, hypothyroidism and increased intracranial pressure etc[3]. High blood pressure is an important risk factor for atherosclerosis; a disorder that involves hyaline and degenerative changes affecting both the intima and media of small arteries and arterioles. The risk of atherosclerosis increases progressively with increasing blood pressure[4]. Cardiovascular diseases and particularly coronary artery disease, remains the leading cause of mortality worldwide, despite recent substantial declines. Hypertension, long recognized as a risk factor for both stroke and myocardial infarction, is an important target for preventive intervention. However, effective hypotensive therapy produces incomplete cardioprotection and most events that would have occurred in the natural state continue to occur among controlled hypertensive patients[5].

It has been seen that hyperuricemia is commonly associated with obesity, hypertriglyceridaemia and hypertension. It was previously thought that hypertriglyceridaemia of primary gout is strongly associated with obesity or alcohol consumption and not with hyperuricemia itself. The incidence of hypertension in the non-gouty population is correlated with age, sex and obesity[5]. But recently, elevation of serum uric acid has been found to be associated with subsequent morbidity and mortality in the general population among patients with congestive heart failure, diabetics and hypertensive patients[6]. Dyslipidaemia is also considered as one of the risk factors linked to serum uric acid[7]. The probable mechanism is that uric acid stabilizes platelet aggregation and enhances thrombotic tendency.

Serum uric acid is associated with body mass index (BMI). Some of the univariate relation of serum uric acid to blood pressure may be due to the strong relation of body mass to both serum uric acid and blood pressure. A low order significant relation between serum uric acid and blood pressure remains with control for body mass index[8].

Uric Acid is the end product of purine metabolism in humans. Humans convert the major purine nucleosides, adenosine and guanosine to uric acid via intermediates[9]. Overproduction of uric acid causes gout. The disease gout, long erroneously thought to be due to "high living", is a disease of the joints, usually in males, caused by an elevated concentration of uric acid in the blood and tissues. The precise cause of gout is not known, but it is suspected to be due to a genetic deficiency of one or another enzyme concerned in purine metabolism[10].

Overproduction of uric acid and extreme hyperuricemia may also lead to a rapidly progressive form of renal insufficiency. Patients with less severe but more prolonged forms of hyperuricemia are predisposed to a more chronic tubulointerstitial disorder, often referred to as gouty nephropathy. Since other conditions associated with hyperuricaemia, such as hypertension, nephrolithiasis, pyelonephritis and even lead poisoning may contribute to renal damage. The effect of chronic hyperuricaemia on renal function is unclear. Nevertheless, the severity of renal involvement in this disorder correlates well with the duration and magnitude of the elevation of the serum uric acid concentration[11].

Hyperuricaemia leading to hyperuric aciduria may also result in increased prevalence of nephrolithiasis[5]. The biochemical hallmark and prerequisite of gout is hyperuricaemia. The balance between rates of production and elimination determines the concentration of uric acid in body fluids. Hyperuricaemia may be due to an excessive rate of uric acid production, a decrease in the renal excretion of uric acid, or a combination of both events.

Hyperuricaemia and gout may be classified as metabolic or renal. Both types of hyperuricaemia may be primary or secondary. Primary refers to those cases in which hyperuricaemia is the central manifestation of the disease. Secondary hyperuricaemia refers to those cases, which develop in the course of another disease or as a consequence of drugs[5].

## SUBJECTS AND METHODS

Previously diagnosed patients suffering from essential hypertension were randomly selected from the PGMI, SIMS, Lahore. Out of these essential hypertensive patients 50 obese and 50 non-obese patients were included in the study. Control healthy individuals, 100 in number, were selected amongst the staff of PGMI, SIMS, Lahore.

Both controls and essential hypertensive patients suffering from diseases like diabetes mellitus, cardiovascular diseases, kidney disorder, and hepatic disorders were not included.

Informed consent was obtained from all the patients and controls. Blood was drawn from the controls as well as essential hypertensive patients after an overnight fast of 10-12 hours. Serum was separated and stored at -20°C till further analysis. Serum TG, total cholesterol, HDL-c, and uric acid were determined by enzymatic colorimetric method. The kits were procured from Clonital diagnostics, Badalona, Spain[12-17]. Serum LDL-c and VLDL-c was calculated by using Friedewald[18] and Wilson's[19] formulae respectively.

## RESULTS

The essential hypertensive patients and the control healthy individuals both had an equal male to female sex distribution ratio. There was no significant change in age of the two groups however, a highly significant change was found in BMI of essential hypertensives when compared with control (Table 1).

Table 2 shows the comparison of age, sex and BMI in control, obese and non-obese essential hypertensive patients. No significant difference between the ages of the control, obese and non-obese essential hypertensive patients was found whereas a significant difference in BMI was found when obese and non-obese essential hypertensive patients were compared with control group.

In Table-3 data of both control and essential hypertensive patients is summarized. The data shows that the mean serum TG, LDL-c, VLDL-c and serum uric acid in the patients were 169.12± 10.16 mg/dL, 122.22 ± 1027 mg/dL, 37.54 ± 3.67 mg/dL and 6.51 ± 1.45 mg/dL respectively and were significantly higher (p<0.001) when compared with controls. The cholesterol and HDL-c were found to be 182.12 ± 10.16 mg/dL and 53.16 ± 6.34 mg/dL respectively and were slightly significant (p<0.005) when compared with controls.

Similarly Table-4 reveals serum uric acid and lipid parameters of the normal healthy individuals (n=100), obese (n=50) and non-obese (n=50)

**Table 1:** *Age, sex and BMI in controls and essential hypertensive patients.*

| Subjects | Age (years) | Sex (male/female) | BMI Kg/m²) |
|---|---|---|---|
| Control (n=100) | 55.56±10.23 | 50/50 | 23.32±2.65 |
| Essential hypertension patients 57.88±10.11# (n=100) | 50/50 | 30.63±3.78 | |

# Non Significant when compared with Control; **p<0.001 when compared with Control

**Table-2:** *Age, sex and BMI in controls, obese and non-obese essential hypertensive patients.*

| Subjects | Age (years) | Sex (male/female) | BMI Kg/m²) |
|---|---|---|---|
| Control (n=100) | 55.56±10.23 | 50/50 | 23.32±2.65 |
| Obese (Essential hy pertension) (n=50) | 54.10±8.32# | 26/24 | 38.50±1.77** |
| Non-obese(essential hypertension) (n=50) | 56.00±9.67# | 24/26 | 22.66±2.26#+ |

# Non Significant as compared to Control; Non-Significant as compared to Obese; **p<0.001 as compared to Control; ± p<0.001 as compared to Obese

**Table 3:** *Lipid Parameters and Serum Uric Acid in Control and Essential Hypertensive Patients.*

| | Control (n=100) | Essential Hypertensive Patient (n=100) |
|---|---|---|
| TG (mg/dL) | 143.99±10.13 | 169.12±10.16 |
| T. Cholesterol (mg/dL) | 171.25_17.61 | 182.12±10.16 |
| HDL-c (mg/dL) | 62.64±7.06 | 53.16±6.34 |
| LDL-c (mg/dL) | 106.69±11.17 | 122.22± 10.27 |
| VLDL-c (mg/dL) | 31.80 4.76 | 37.54±3.67 |
| S. Uric Acid (mg/dL) | 4.72±1.83 | 6.51 ± 1.45 |

**p<0.001 when compared with Control: p<0.005 when compared with Control

**Table 4:** Lipid parameters artd serum uric acid in control obese and non-obese essential hypertensive patients.

| | Control (n=100) | Obese (n=50) | Non-obese (n=50) |
|---|---|---|---|
| TG (mg/dL) | 143.99±10.13 | 172.87±13.05 | 162.13±10.51 |
| T. Cllolesterol (mg/dL) | 171.25±17.61 | 188.87±17.12 | 191.17±16.23 |
| HDL-c (mg/dL) | 62.64±7.06 | 48.39_8.01 | 53.12_6.40 |
| LDL-c (mg/dL) | 106.69±11.17 | 126.16±10.12 | 118.29±10.67 |
| VLDL-c (mg/dL) | 31.80±4.76 | 35.47±3.76 | 32.51 ±4.67 |
| S. Uric Acid (mg/dL) | 4.72±1.83 | 6.98±1.51 | 6.04±1.31 |

p<0.01 compared to Control; ** p<0.001 compared to Control; p<0.001 compared to Obese; # NonSignificant compared to Obese; A p<0.001 compared to Obese; C p<n ool compared to Obese; B NonSignificant as compared to Control; D p<0.001 compared to Obese.

hypertensive patients. This is evident from the table that serum TG in obese and non-obese was found to be 172.87 ± 13.05 mg/dL and 162.13± 10.51 mg/dL respectively. A highly significant

difference in TG of obese was found when compared with controls. However a significant change amongst non-obese and control and obese and non-obese themselves was found. Serum cholesterol shows a highly significant change (p<0.001) for both obese and non-obese essential hypertensive patients when compared with controls however non-significant difference among themselves i.e. obese and non-obese patients was found. Serum HDL-c, LDL-c and VLDL-c (mg/dL) in obese and non-obese groups were found to be 48.39 ± 8.01, 53.12 ± 6.40, 126.16 ± 10.12, 118.29± 10.67 and 35.47 ± 376, 32.51 ± 4.67 respectively. In both obese and non-obese groups a highly significant change was noticed for the above parameters when compared with controls respectively. A highly significant difference for HDL-c and LDL-c between the obese and non-obese essential hypertensive patients was found (p<0.001) however insignificant change for VLDL-c between the two groups was noticed. Serum uric acid amongst the controls, obese and non-obese was noticed to be 4.72±1.83 mg/dL, 6.98 ±1.51 mg/dL and 6.04±1.31 mg/dL respectively There was a highly significant difference in the serum uric acid levels for obese and non-obese patients when compared with controls (p<0.001). A similar change was observed in serum uric acid of obese patients when compared with non-obese essential hypertensive patients.

## DISCUSSION

In clinical and epidemiological studies serum uric acid has been found to be related not only to risk of gout, but also to risk of hypertension, coronary heart disease, and diabetes mellitus[8]. However the role of serum uric acid in the pathogenesis of these latter diseases is still unclear[20-22]. Hypertension is sustained elevation of systemic arterial pressure[1]. The adverse effects of hypertension principally involve the central nervous system, the retina, the heart and the kidneys[23]. Recently it has been found that essential hypertension may also be associated with hyperuricaemia with normal renal functions[24-28]. It is also associated with BMI, triacylglycerides, and serum glucose[8].

Hyperuricaemia is predictive for the development of both hypertension and coronary artery disease; it is increased in patients with hypertension, and when present in hypertension, an elevated serum uric acid is associated with increased cardiovascular morbidity and mortality. As serum uric acid carries prognostic informations it should be measured in patients at risk for essential hypertension[29].

Various studies suggest that serum uric acid levels are affected by both genetic and environmental factors and related to such biological factors as gender, age and body mass[30-32]. Milionis *et al.,* showed a positive association between hypertension and serum uric acid, whereas a few have failed to reveal such association[33].

Data on serum uric acid levels in essential hypertensive patients in Pakistani population are sparse. So a need was felt to find out association between serum uric acid and hypertension in Pakistani population. For this purpose hundred hypertensive patients, with an equal male to female ratio were selected for the study and results were compared with normotensive controls. The data was analyzed and it was found that serum uric acid levels were significantly higher (p<0.001) in the study group as compared to the controls (table 3).

By comparing the levels of serum cholesterol, it was seen that they were higher in the study group as compared to controls. This change was markedly significant (p<0.005). Similar results were also reported by previous workers[8]. Further it was found that serum triacylglycerides were higher in patients when compared with controls. The difference was significantly higher (p<0.001). The same has been reported by Savage and co-workers[34] and also by others[33]. Apart from hyperuricaemia, hypertriglyceridemia was also associated with hypertension in Japanese-Americans[35]. This is again in agreement with the present findings.

The mean (±SD) HDL-c among the patients were found lower than the controls. The difference between the two groups was markedly significant (p<0.005). Similar trend of results were found by previous workers[8,36,37].

Similarly a highly significant difference (p< 0.001) between the two groups for LDL-c was found in our study population. Our results are in accordance with the previous workers[8]. The maximum mean (±SD) VLDL-c was found among the patients (overall) and these values were significantly higher than the normal individuals (p<0.001). This is again in accordance with the earlier works carried in Begging, China[8].

Although serum uric acid, serum cholesterol, triacylglycerol, LDL-c and VLDL-c were significantly higher in hypertensive patients, but serum uric acid was found to be independently elevated in patients with high blood pressure. Lipid profile may have an effect on levels of serum uric acid[7]. Out of total patients eighteen individuals (18%) showed elevated serum uric acid, however their

lipid profile was normal when compared with controls. This is in accordance with the previous results[29-35].

A group of workers in Japan found in a proportional hazard analysis that hyperinsulinaemia, hyperuricaemia, obesity and hypertriglyceridaemia were significantly associated with hypertension[35]. In USA, Alderman performed a multivariate analysis and found that cardiovascular disease incidence was significantly associated with serum uric acid with a hazard ratio of 1.22, controlling for other known cardiovascular risk factors, including serum creatinine, body mass index, and diuretics[28]. Despite blood pressure control, serum uric acid level increased during treatment. The serum uric acid was significantly and directly associated with cardiovascular disease events, independently of diuretic use and other cardiovascular risk factors.

In **conclusion** it is seen that the results of present study are comparable to most studies performed in different parts of the world showing significant increase in the levels of serum uric acid in hypertensive patients when compared with normal individuals.

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