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To Study the Biochemical Changes For Prediction of Essential Hypertension

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Abstract

Background: In industrialized countries, hypertension is the fourth leading cause of death, but in underdeveloped countries, it is the seventh leading cause of death. Hypertension, defined as a systolic BP of 140 mmHg or a diastolic BP of 90 mmHg, is responsible for roughly 7.1 million deaths worldwide each year. Hypertension is a crucial independent prognosticator of cardiovascular disease, cerebrovascular accidents and death. In 2008, 17.3 million people died from CVDs, accounting for 30% of all global deaths. Over 80% of CVD deaths occur in low- and middle-income countries, and men and women die in nearly equal numbers. It is predicted that cardiovascular diseases will spread fast in India, with the country accounting for more than half of all heart disease cases in the world within the next 15 years. The current study was conducted to determine the relationship between hyperuricemia and EHT in the Central Indian population.

Aim: To establish the significance of Biochemical Changes in the prediction of essential hypertension.

Material and Method: A total of 250 people took part in this cross-sectional hospital-based case control study. All of the subjects were recruited at random from the Medicine OPD, attendants or family members of established hypertension patients, and healthy volunteers such as clinical and nonclinical personnel of a tertiary care hospital, as well as people who came to the hospital for a health examination. All of the age and sex matched subjects (20-50 years old) were separated into three groups: 70 subjects with normal blood pressure made up the control group. 90 cases of prehypertension were included in the Pre-HT group. 90 patients of newly diagnosed essential hypertension were included in the HT group. JNC7 criteria are used to determine the diagnosis of PreHT and EHT. Using commercially available reagents or kits, the levels of serum uric acid (SUA), serum malondialdehyde (MDA), lipid profile, serum creatinine, and fasting blood glucose were determined. The levels of serum creatinine and fasting blood glucose were calculated to rule out renal disease and diabetes mellitus, respectively.

Results: The significantly increased trend in mean serum uric acid level was observed from control to prehypertensive to hypertensive cases. This study showed that hypertensive cases had significantly higher level of

MDA than prehypertensive and control group. Among lipid profile parameters the significantly increasing trend was observed in mean value of TC, LDL, VLDL and TGL from control to prehypertensive to hypertensive cases whereas decreasing trend was observed in mean value of serum high density lipoprotein (HDL) from control to prehypertensive to hypertensive cases.

Conclusion: As a result, our findings suggest that regular monitoring of blood pressure, serum uric acid, and lipid levels, as well as preserving oxidative balance in hypertensive patients, could assist to avoid CVD and other hypertension-related disorders. The progression of disease could be slowed by providing proper education to patients about a healthy lifestyle and encouraging them to engage in activities such as yoga, aerobics, and walking, among other things.

Keywords: Uric Acid, MDA, CVD and Hypertension

Introduction

Hypertension is a major public health concern around the world, and it is still the most well-known risk factor for cardiovascular morbidity and mortality. The WHO report 1998 denotes that regarding the prevalence of any disease, hypertension places forth in the world.(1) It affects one in every three adults worldwide(2), amounting to approximately one billion people in absolute numbers in 2000, with the figure expected to rise to more than 1.5 billion by 2025.(3) Population demographic changes, economic development, globalisation, increased food availability, and decreased physical activity are thought to be the key drivers of this rapid rise in hypertension.(4) Hypertension has long been recognised as a major public health issue in both developing and industrialised countries. The rising prevalence of hypertension, which leads to cardiovascular ailments, is a recognised public health issue in India.(5) In both urban and rural parts of India, the prevalence of hypertension is on the rise.

Prehypertension as the name hints that it predates hypertension. Persons with prehypertension have been demonstrated to be at augmented risk of developing hypertension. The increased risk linked with high-normal pressures was the focus of the JNC 7. The principal objective of the new classification system is to increase the alertness and lifestyle alterations in prehypertensive people with this increased risk. In most of cases, hypertension is idiopathic and is named as essential or primary hypertension. Essential hypertension has been appropriately addressed as the silent killer because it is generally asymptomatic and hidden. Although the cause of most of the hypertension is not acknowledged, some people have risk factors that give them a larger risk of getting hypertension.(6)

Hypertension is a serious health problem, especially because it is asymptomatic. The majority of patients with uncomplicated hypertension are asymptomatic. They are revealed to have hypertension by chance. Severe headache, nausea, visual problems, dizziness, and even renal failure are signs of life-threatening hypertension, such as malignant hypertension. Hypertension can impact nearly all of the body's critical organs. Patients with advanced hypertension may have signs and symptoms that point to an organ in jeopardy. Palpitations, fatigability, impotence, epistaxis, hematuria, blurring of vision, weakness, dizziness, angina pectoris, and dyspnea are some of the symptoms.(7)

The progression of both hypertension and coronary artery disease is predicted by a high serum uric acid level. It is higher in hypertensive patients, and when hyperuricemia is present, it is associated with greater cardiovascular morbidity and mortality. At least in adolescents, hyperuricemia is more common in primary hypertension than secondary hypertension. This suggests that the strongest link between uric acid and hypertension is found in people who have

recently developed essential hypertension.[8] Consequently, if hyperuricemia leads to hypertension, the presumption is that it should contribute to prehypertension (PreHT) as well. Given that prehypertension is the precursor to hypertension, it's reasonable to assume that HU will be more prevalent among those with prehypertension. Furthermore, as serum uric acid carries prognostic information it should be evaluated in patients at risk for essential hypertension.[9]

Traditional modifiable risk factors have been thoroughly investigated, but there is an urgent need to uncover other therapeutic risk factors that are simple to assess and widespread in the general population. Hyperuricemia may be a controllable and treated risk factor that can help to prevent the occurrence of hypertension. Furthermore, the importance of SUA and S. MDA levels in the prediction of essential hypertension in PreHT and EHT has never been investigated in southern Rajasthan, which is why the current study was undertaken to determine the significance of serum uric acid and serum MDA levels in the prediction of essential hypertension.

Material and Methods

All the subjects were chosen randomly from Medicine OPD, attendants or family members of established hypertensive patients and healthy volunteers like clinical and nonclinical staff of a tertiary care hospital and individuals comings to hospital for health checkup.

Inclusion criteria: All the age matched (20-50 years old) and sex matched subjects were broadly divided in to three groups:

- **Control group:** 70 subjects with normal blood pressure or any other condition known to cause hyperuricemia.
- **PreHT group**: 90 cases of prehypertension
- **HT group**: 90 cases of essential hypertension that were newly diagnosed. JNC7 criteria are used to determine the diagnosis of PreHT and EHT.

Exclusion criteria: Hypertensive patients who are pregnant (Gestational hypertension) Renal abnormalities, metabolic disorders, fluid volume changes, endocrine problems, and other causes of secondary hypertension Gout is a type of arthritis that affects the joints Diabetes mellitus patients, smokers, and alcoholics Antihypertensive, lipid-lowering, and hypouricaemic medications are being used by the patient.

After receiving ethical approval, all subjects signed a written voluntary informed consent form after being informed about their involvement in the study in their native language. Then all the subjects will be screened for:

Demographical History: - Age, sex, marital status.

Medical History: - Diabetes mellitus, family history of hypertension, cardiovascular diseases, metabolic disorders, endocrinal disorders, gout and renal diseases.

Life Style Factors: - Vegetarian/Non vegetarian, Smoking habits, alcohol consumption and physical activity

Sample Collection

All of the data from the three groups, as well as the necessary physical examination, was collected in a thorough proforma. After diagnosis, all individuals had a blood sample (5 ml) collected into a simple vial by antecubital vein puncture after an overnight fast (12 hrs). After that, set it aside for 30 minutes at room temperature. Serum was separated by centrifugation at 3000rpm for 10 minutes after blood clotting. Following that, the serum sample was transferred to a simple container for biochemical examination.

Methods:

- Serum Uric Acid: By Modified Trinder Method. [10]
- Serum Lipid Profile

1. Total Cholesterol (TC): By Cholesterol oxidase phasphaaminoantipyrine (CHOD–PAP) method [11]
2. High Density Lipoprotein Cholesterol (HDL-C): Phosphotungstic Acid Method [12]
3. Very Low Density Lipoprotein Cholesterol (VLDL-C): By Friedewald's formula[13]
4. Low Density Lipoprotein Cholesterol (LDL-C): By Friedewald's formula.[13]
5. Triglyceride (TG): By GPO – Trinder Method [10]

- Serum Malondialdehyde (MDA): Thiobarbituric acid (TBA) assay method [14]
- Serum Creatinine: By Jaffe's method [15]
- Fasting Blood Glucose level: Enzymatic method by using Glucose oxidase (GOD) and Peroxidase [16]

Statistical Analysis:

The data was analyzed by using Statistical Package for the Social Sciences (SPSS) Version 16.0. Significance testing of difference for mean ± SD of three groups was done by Analysis of variance test (ANOVA).

Result:

Table 1: Comparison of Serum Uric acid, MDA, creatinine and fasting blood glucose levels among different groups

Variables	Control Group	Pre HT Group	HT Group
Uric acid (mg/dL)	5.27±0.34	6.80±0.77	7.61±0.86
MDA (nmol/mL)	1.84±0.22	2.47±0.33	2.79±0.52
Creatinine(mg/dL)	65.41±1.28	85.44±0.55	96.73±3.86
FBS (mg/dL)	0.53±0.15	1.11±0.69	1.92±43.25

In the present study, the difference in mean ± SD of uric acid level and MDA, creatinine and fasting blood glucose levels between control, PreHT and HT group were found to be highly significant. Further the mean ± SD of S. uric acid level and S. MDA level of hypertensive group was found to be significantly higher as compared to prehypertensive & control group.

Table 2: Comparison of plasma lipid profile levels among different groups.

Lipid profile parameter (mg/dl)	Control Group	Pre HT Group	HT Group
Total Cholesterol	183.59±76.81	248.36±32.51	285.55±22.59
High-density lipoprotein	43.48±6.86	39.28±6.66	38.09±6.97
Low-density lipoprotein	117.92±18.04	175.37±35.72	206.64±30.19
Very low-density lipoprotein	25.18±5.57	37.64±5.78	47.90±15.72
Triglycerides	120.14±24.34	175.18±26.77	209.28±68.52

The results showed that the difference in mean ± SD of serum TC, HDL-C, LDL-C, VLDL-C and TGL were found to be highly significant between hypertensive, prehypertensive & control group. The mean ± SD value of serum TC, LDL-C, VLDL-C and TGL were increasing from control to PreHT group to HT group

Discussion

Hypertension posing a major public health challenge to the universe in socioeconomic and epidemiological transition. It is one of the leading risk factors for cardiovascular mortality, which explains 20–50 per cent of all deaths. The etiological factors linked with hypertension are difficult to pretend because hypertension results from a complex interplay of genes and environmental factors (**Colledge NR et al, 2010**)[17]. Raised serum uric acid level is associated with increased cardiovascular morbidity and mortality rate (**Jawed SAMIA et al, 2005**)[18].

In this study we found that the mean ± SD of serum uric acid level in hypertensive group was significantly higher as compared to prehypertensive & controls. In favor of our study **Assob JCN et al, 2014**[19] observed that the serum uric acid level in prehypertensive group was significantly higher than the control group. A prospective study, done by **Weilizhang et al, 2009**[20] in a Chinese community also support our results.

Raised level of serum uric acid (SUA) has been associated with an amplified risk for the development of essential hypertension (**Selby JV et al, 1990**[21]**; Cannon PJ et al, 1966**[22]). Serum uric acid levels have been coupled cross-sectional with BP (**Feig DI, Johnson RJ, 2003**[8]) and longitudinally with hypertension incidence (**Kahn HA et al, 1972)**[23] and future increase in BP (**Masuo K et al, 2003).**[24]

The increase in serum uric acid concentration within hypertension may be due to the decrease in renal blood flow and early hypertensive nephrosclerosis that accompanies the hypertensive state, since a low renal blood flow will inspire urate reabsorption (**Messerli FH et al, 1980)**[25]. A study done by **Amirkhizi F et al, 2007**[26] found that there was an increase in the MDA level (a marker of lipid peroxidation), in the prehypertensive group in comparison to control group. In favor of our study **Kashyap et al, 2005**[27] showed that, essential hypertension is associated with greater than normal level of MDA or lipid peroxidation and an imbalance in antioxidant status suggesting that oxidative stress is important in the pathogenesis of essential hypertension or in arterial damage related to essential hypertension. The degree of cellular damage and aging depend upon the balance between production of oxidants and the removal by the antioxidant system. Amongst different antioxidant mechanisms, superoxide dismutase (SOD) and catalase play important role in belittling the levels of free radicals (**Kornatowska KK et al, 2004)**[28]**.**

Our findings were corresponding to the study of **Kumar NL et al, 2010**[29]who studied the role of lipid profile, serum Mg^{+2} and blood glucose in hypertensive and control individuals of Rajahmundru, Andhra Pradesh, India. Their study revealed analogous findings of elevated serum TC, LDL-C, VLDL-C and triglycerides as observed in our study. On contrary to our study, in case of serum HDL-C level, they obtained no significant decrease between hypertensive and control. These results point out that dyslipidemia is linked with hypertension.

Plasma lipid profile, that is changed in hypertensive patients (**Steinberg D et al, 1989)**[30] appears to be a significant factor in the development of premature atherosclerosis and includes an increase in TC, LDL-C and decrease in HDL-C and phospholipids. Abnormalcies in lipid profile predate the occurrence of stage I hypertension from prehypertension, so it is wise to advocate lipid profile as screening of asymptomatic prehypertensive patients. Moreover, dyslipidemia is not rare in hypertensive; therefore hypertensive patients require measurement of BP and lipid profile at regular intervals all through their primary health care to stop further provocation and risks of coronary artery diseases (CAD) and stroke

Conclusion:

To summarise, a high amount of SUA is strongly associated to PreHT and EHT. When compared to prehypertensive and normotensive controls, the mean blood uric acid level and the incidence of hyperuricemia were considerably higher in newly diagnosed cases of hypertension. Furthermore, SUA was found to be positively and significantly linked with SBP in newly diagnosed instances of hypertension, and patients with PreHT and EHT frequently had hyperuricemia as a co-morbidity, even when they were not on medication. These findings suggest that measuring serum uric acid levels in clinical practise may aid in detecting the risk of developing essential hypertension. Furthermore, there is a possibility that hypertension can be managed in the future by lowering SUA levels as a modifiable risk factor, particularly in new and recent onset primary hypertension.

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