Original Article

Early Management of Hyperuricemia Might Delay the Development of Essential Hypertension.

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Abstract

Background: *In the 21st century, the prevalence pattern of hypertension in different developing countries differs from developed countries. Persistent hypertension is one of the risk factors and is the leading cause of heart disease, chronic kidney disease (CKD) & cerebrovascular disease. Even mild to moderate essential hypertension usually causes significant renal function impairment only after several years.* ***Objectives:*** *To assess the serum uric acid level in hypertensive patients and compare the findings with those found in normotensive people.* ***Materials & Methods:*** *This case-control study was done at the Department of Biochemistry, Mymensingh Medical College, Mymensingh during the period of January 2010 to December 2010. A total of 143 subjects of both sexes were selected for the purpose. Out of them, 73 were the case and 70 were the control. The subjects were classified into the following groups; Group I includes 73 were essential hypertensive subjects. Group II includes 70 were healthy adults. All statistical parameters analysis were done by SPSS 12.0 version; P-value<0.05 was considered as significant.* ***Results:*** *There was a significant (P<0.05) increase in blood urea in subjects with hypertension compared to that of the control.* ***Conclusion:*** *Evaluation of uric acid before and during treatment of hypertension is required to identify as a risk factor.*

Keywords: *Essential hypertension, Hyperuricemia, Renal function, Chronic renal disease (CKD).*

Date of received: *14.05.2021*

Date of acceptance: *20.08.2021*

DOI: https://doi.org/10.3329/kyamcj.v12i3.56551

KYAMC Journal. 2021;12(3): 117-121 .

Introduction

Hypertension (HTN) or high blood pressure is a chronic medical condition in which the blood pressure is higher than normal (systolic >130 mm of hg & diastolic is >80 mm of hg). About 90-95% of cases are termed primary hypertension, which refers to high blood pressure for which the medical cause is still unknown. The remaining 5-10% of cases (secondary hypertension) are caused by another medical condition that affects the kidneys, arteries, heart or endocrine system.[1] Hypertension is now recognized as a significant clinical and public health problem globally. A few decades back, before any epidemiological research, 'hypertension' was considered a disease rather than a risk factor.[2] The pattern of hypertension in developing countries differs from that in the developed countries. Very few studies in Bangladesh have shown an upward trend in the prevalence of hypertension. The incidence of hypertension in the subcontinent increased by 30 times among the urban and about ten times among the rural population over the last 50 years. Hypertension is the most familiar cardiovascular disease worldwide, including Bangladesh. Cardiovascular diseases are also emerging health problems in Bangladesh. Surveys indicate that 15- 20% of the adult population (18 years and above) in Bangladesh suffers from hypertension. Some study results show that 70% of strokes, 23.8% of myocardial infarction and heart failures and 11% of renal failures are due to hypertension in Bangladesh.[3-5]

Some factors might have contributed to this rising trend of hypertension: the consequences of change in lifestyle patterns like diet, stress, and increased population have been

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implicated.[6] Though the majority of the patients may remain asymptomatic and left untreated ;the complication may develop and become fatal. Nevertheless still, this disease is readily being detectable and treatable. Early management of hypertension can significantly reduce cardiovascular morbidity and mortality.[7] It is also known that hypertension is genetically predominant which, caused by more than one gene. Hypertension usually occurs with other metabolically linked risk factors, and less than 20% occurs in isolation.[8] There is a cluster of these risk factors with hypertension, so physicians should routinely screen the organ function test for the presence of these risk factors. In this report, we review the epidemiological evidence and potential mechanism for this association between uric acid and hypertension.

The role of uric acid in hypertension was first discovered in 1874, yet its role in this condition remains unclear. It remains possible that uric acid is a marker for xanthenes oxidase-associated oxidants, driving the hypertensive response. However, this evidence suggests that uric acid is a true modifying and possibly causal factor for primary human hypertension. Therefore, health care professionals must not only identify and treat hypertension but also should promote preventive strategies to decrease the prevalence of hypertension. [9,10]

It is also known that hypertension is highly heritable and polygenic (caused by more than one gene), and a few genes have been postulated in the etiology of this condition. Recently, work related to the association between essential hypertension and endothelial damage has gained popularity among hypertension scientists. It remains unclear, however, whether endothelial changes in the development of hypertension.The results from many clinical studies show the relationship between the aggravation of the hypertensive complication and the changes in various chemistries in blood.[11,12]

The current study was undertaken to find out the relationship between hyperuricemia and essential hypertension. Uric acid is the major catabolic end product of the purine bases, produced endogenously or available from the dietary nucleic acid. The daily endogenously synthesis rate of uric acid (UA) is approximately 400 mg; dietary sources contribute another 300 mg.[13] The net urinary excretion of uric acid is 6% to 12% of the amount filtered. A variety of factors influence the renal exertion of uric acid. These include volume status, the rennin-angiotensin system, catecholamine, urinary solute excretion, plasma ketoacids, plasma glucose.[14] Uric acid was first associated with its role in hypertension condition remains unclear. Before the modern age, it was thought uric acid could be a secondary response to hypertension or its associated condition. However, more recent experimental and clinical studies suggest that uric acid could contribute to hypertension's pathogenesis, mediated by several mechanisms such as inflammation, vascular smooth muscle cell proliferation in the renal microcirculation, endothelial dysfunction, and activation of rennin angiotensin system. [15,16] Hypertension is prevented by maintaining serum uric acid. The increase in serum uric acid in hypertension may be due to decreased renal blood flow, which will stimulate urate reabsorption.[17] Recent evidence supports a role for uric acid as an actual cardiovascular risk factor, particularly hypertension and renal disease. Increased renal vascular and total peripheral resistances reflecting renal and systemic hypertensive vascular disease paralleled the rising serum uric acid levels. These data suggest that unexplained hyperuricemia in patients with essential hypertension most likely reflects early renal vascular involvement precisely, nephrosclerosis.[18,19]

Materials & methods

This case-control study was conducted in the Department of Biochemistry,in collaboration with the Department of Internal Medicine, Mymensingh Medical College& Hospital, Mymensingh,from January 2010 to December 2010. Ethical clearance for the study was taken from the central ethical committee of Mymensingh Medical College and Hospital Mymensingh. A total of 143 patients were selected for this study who had visited the outpatient medicine department of MMCH; out of the 73 were cases, and 70 were selected as a control study group. A well-planned data sheet was constructed for interviewing the subjects based on set inclusion and exclusion criteria. Purposive (non-random) and convenient sampling technique has been followed. The purpose and procedure of the study were explained in detail, and informed written consent was taken from all the study subjects. All the information of the study subjects, including history, clinical findings, were recorded in preformed datasheets; BP was measured by using a standard sphygmomanometer after 10 minutes of rest in a quiet room according to the recommendation of the British Hypertension Society. The mean of two measurements taken 5 minutes apart was recorded. Inclusion criteria for case and control, respectively, are between 30 to 55 years of both sexes. Diagnosed essential hypertensive patients(SBP>=140mmHg; DBP>=90mmHg).Known hypertensive patients but are normotensive by taking drugs. Healthy normotensive adult.SBP:≤ 120;DBP:≤ 80. Then blood samples were collected from the study subjects to estimate serum uric acid.. After all, statistical analyses were processed by computer software SPSS (Statistical Package for Social Science) version 12. The mean value of the findings has been presented by unpaired "t" test and x^2 (chi-square) test. For analytical tests, the level of significance was 95% confidence limit ($p < 0.05$) was taken as the level of significance.The test statistics to be used to analyze the data are descriptive statistics. The summarized data were presented in the form of a table.

Results

In this study, Comparing the serum uric acid in group I and group II shows, the mean (± SD) serum uric acid levels in group I (case group) and that of the subjects without hypertension (group II) were 5.26 ± 0.69 and 4.85 ± 0.56 mg/dl respectively (Table I and Fig.1). "t" value: 2.789; Df: 141 ; P value less than 0.05 was taken as the level of significance. There was a significant ($p<0.001$) increase of serum uric acid in subjects with hypertension compared to that of the control. Distribution of serum uric acid in study subjects showing that, in case group serum uric acid level < 6.5 mg/dl

was 59 (80%) subjects and ≥ 6.5 mg/dl was in 14 (19%) subjects. In control group, serum uric acid level was < 6.5mg/dl in 66 (94%) subjects and ≥ 6.5 mg/dl in 04(6%) subjects. The distribution showed significance difference between case and control group ($p<0.05$) . Chi-Square: 5.887 Degrees of freedom (df): 1, figures in parenthesis show percentage.(Table II & Fig. 2).

Table I : Serum uric acid levels in hypertensive and normotensive subjects

Biochemical Variables	Group - I n=73 Mean ± SD	Group - II n=70 Mean ± SD	P value
Serum uric acid (mg/dl)	5.26 ± 0.69	4.85 ± 0.56	<0.001

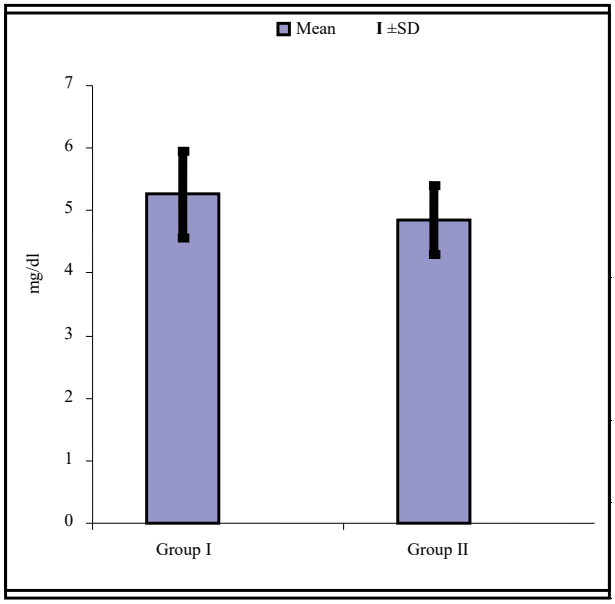

Fig. 1: Showing serum uric acid levels in hypertensive and normotensive subjects.

Table II : Distribution of serum uric acid level in the study subjects

Range	Frequencies		P value
	Group I	Group II	
<6.5 mg/dl	59 (80 %)	66 (94 %)	0.015
≥6.5 mg/dl	14 (19%)	04 (6 %)	
Total	73 (100 %)	70 (100 %)	

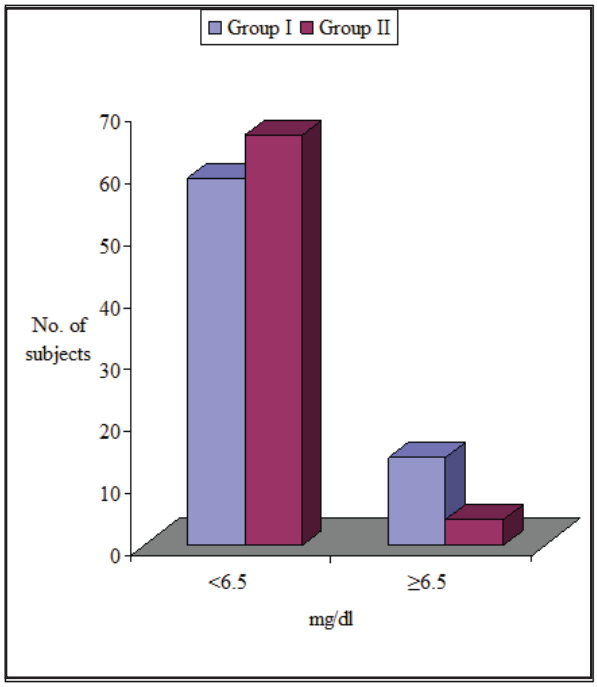

Fig 2: Showing distribution of serum uric acid level of the study subjects

Discussion

Hypertension (HTN) or high blood pressure is a chronic medical condition when the systemic arterial blood pressure is elevated. Monitoring renal function before and during treatment of hypertension may provide an option to understand the problems and help prevent serious adverse effects. Early changes in biochemical parameters may be significant and indicate the need for more frequent monitoring. Renal function is an essential predictor in hypertensive patients at high risk. Variable results are found in the case of serum uric acid. The present study was designed to observe the changes of serum uric acid in essential hypertensive patients from this view.In the present study, an assessment of serum uric acid in hypertensive patients was observed. Initially, serum uric acid in study subjects was estimated by us. Then a comparison was made between group I and group II. This study identified a higher level of uric acid found in essential hypertensive

patients than those who are normotensive. In this study, raised uric acid level in the case group may be associated with the acceleration of pathophysiology of hypertension. This finding is in agreement with those of the following observations.[20- 22]

The result of our study also agreed with Mehmet et al.[15] They explained that uric acid is a maker for xanthine oxidase-associated oxidants, which could drive hypertensive responses. So the evidence suggests that uric acid is a true modifying and possible causal factor for primary human hypertension. Similarly another study describes[23] a significant positive interrelationship between high uric acid levels in hypertension. Increased renal vascular and total peripheral resistance reflecting renal and systemic hypertensive vascular disease rising serum uric acid level might be involved in the genesis of hypertension rather than a simple marker of hypertension. So the result of our study also states that serum uric acid levels increased in hypertension .

However, the result of our study is not consistent with those by Daniel et al.[18], They did not find any heterogeneities of the result, due to various studied population different inclusion and exclusion criteria and methods also.

Conclusion

From the statistical analysis of the result obtained in the present study and their comparison with those of the pre-existing reports, it may be concluded that there were significant alterations in serum uric acid levels in hypertensive subjects. Therefore, monitoring serum uric acid before and during treatment of hypertension may provide an idea to understand the problems and help prevent the early onset of hypertension. Furthermore, it is needed to reinforce the investigations of this parameter in daily practice.

Limitation of the study

This study was done within the content of the facilities available to us. Cystatin C was not observed. Because of time and financial constraints, we had to conduct this case-control study with a small population size.

Acknowledgement

We would like to thank those who actively participated in this study and the members of Institutional Review Board, MMCH for their kind permission and cordial support.

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