Section: Biochemistry

Original Research Article

STUDY OF SERUM URIC ACID AND VITAMIN-D LEVELS IN PATIENTS WITH ESSENTIAL HYPERTENSION AT M.G.M. MEDICAL COLLEGE, KISHANGANJ

Rakesh Kumar Sinha[1], Abrita Choudhury[2]

[1]Senior Resident, Department of Biochemistry, AIIMS, Patna, India.
[2]Assistant Professor, Department of Biochemistry, MGM Medical College & LSK Hospital, Kishanganj, Bihar, India.

Received : 17/06/2023
Received in revised form : 20/07/2023
Accepted : 01/08/2023

Keywords:
Essential hypertension, serum uric acid, vitamin D, biomarkers, blood pressure, cardiovascular disease.

Corresponding Author:
Dr. Rakesh Kumar Sinha,
Email: docsinha1@gmail.com.

DOI: 10.47009/jamp.2023.5.4.271

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5(4); 1352-1357

Abstract

Background: Essential hypertension is a prevalent cardiovascular disorder characterized by elevated blood pressure levels, contributing significantly to the global burden of disease. Serum uric acid and vitamin D have been suggested as potential biomarkers and contributors to hypertension development. This study aims to investigate the association between serum uric acid and vitamin D levels in patients with essential hypertension at M.G.M. Medical College, Kishanganj. **Materials and Methods:** A Case-Control study was conducted involving 50 Patients of Essential Hypertension between the age group of 25-75 years satisfying inclusion and exclusion criteria visiting medicine OPD & IPD of M.G.M Medical College. All patients were re-categorised into Stage-I and Stage-II hypertension according to JNC (VII) criteria. All patients were undergoing different examinations during the period September 2018 to August 2020. Clinical and demographic data were collected, and statistical analysis was performed to assess the relationship between serum uric acid, vitamin D, and essential hypertension. **Results:** In the present study the mean age of patients in hypertension group and control group is 52.960 (+ 11.67) years and 41.940(+ 12.54) years respectively, The male to female ratio in hypertension group is 1.941:1 and male to female ratio in control group is 1.631:1. Males were significantly more in number as compared to females in both the groups. The mean serum Vitamin D level of patients in hypertension group and control group is 23.140 (+ 5.39) ng/mL and 43.360 (+13.59) ng/mL respectively. Mean serum Vitamin D level of hypertension group is significantly lower than the control group. In the present study the mean serum uric acid in the hypertensive group was 6.570 (+0.79) mg/dl. On the other hand the mean serum uric acid level in the control group was 4.610 (+0.51) mg/dl. Data analysis by T-test, done to compare the mean serum uric acid values in hypertensive with that of control was proven to be significant with a p value of 0.04. **Conclusion:** Serum uric acid can be used probably as an early biochemical marker to determine the severity of hypertension as stage 2 hypertensive had more elevation in serum uric acid levels as compared to other hypertensive. Thus serum uric acid estimation can be used for aiding in the diagnosis of essential hypertension as well as in assessment of the severity. Vitamin D deficiency may be included as a fifth contributor for hypertension.

INTRODUCTION

Essential hypertension also called primary and idiopathic hypertension is the form of arterial hypertension that by definition has no identifiable cause. It tends to be multi-factorial, and is likely to be the consequence of an interaction between environmental and genetic factors. Prevalence of essential hypertension increases with age, and individuals with relatively high blood pressure at younger ages are at increased risk for the subsequent development of hypertension.

Hypertension is one of the most common complex disorders. The etiology of hypertension differs widely amongst individuals within a large population.[1] And by definition, essential hypertension has no identifiable cause. However, several risk factors have been identified.

ISSN(O):2687-5365; ISSN(P): 2753-6556

Uric acid is an end product of the purine catabolic pathway.[2] and uric acid production is reported to be highest in the liver and intestine.[3] Of note, significant uric acid production has been detected in microvascular endothelial cells from several tissues.[3] At the enzyme level, the breakdown of adenine-based and guanine-based purine compounds depends on the enzyme xanthine oxidoreductase (XOR), the only enzyme capable of producing uric acid.[4]

It serves no biochemical function other than being an end product of purine metabolism, was first discovered in 1776. A Swedish chemist Scheele isolated it from a urinary tract stone. In 1797, a British chemist Wallaston detected uric acid in a tophus which was removed from his own ear. About 50 years later Alfred Baring Garrod, a British physician showed by chemical isolation that uric acid was abnormally high in gouty patients.[5]

Vitamin-D deficiency has been traditionally associated with poor bone growth & development and development of rickets in children and osteomalacia in adults. In recent years emphasis has been given to the role of Vitamin-D in areas beyond those traditionally known.

Vitamin D plays a key role in regulation of blood pressure and in the pathogenesis of hypertension through its effects on calcium homeostasis, vascular smooth muscle, endothelial cells and activity of renin- angiotensin- aldosterone system.[6] Due to the continued interest and lack of information on serum uric acid levels as well as vitamin D levels and the risk of hypertension, this study was conducted to examine serum uric acid and vitamin D level in patients with essential hypertension and their role in etiopathogenesis of essential hypertension.

The prevalence of hypo-vitaminosis D is directly attributable to higher latitudes because of less intense UVB radiation, colder climates due to less skin exposure, and darker skin as it impedes UVB penetration and reduces vitamin D production The fact that a higher incidence of essential hypertension occurs during the winter, in people living in higher latitudes, and in those with deep skin pigmentation living far from the equator.[7] makes it reasonable to speculate that vitamin D deficiency may contribute to increased prevalence of essential hypertension.

MATERIALS AND METHODS

A Case- Control study was conducted involving 50 Patients of Essential Hypertension between the age group of 25-75 years satisfying inclusion and exclusion criteria visiting medicine OPD & IPD of M.G.M Medical College. All patients were re-categorised into Stage-I and Stage-II hypertension according to JNC (VII) criteria. All patients were undergoing different examinations during the period September 2018 to August 2020. Clinical and demographic data were collected, and statistical analysis was performed to assess the relationship between serum uric acid, vitamin D, and essential hypertension.

Inclusion Criteria

1. Fifty essential Hypertension patients attending general medicine OPD, M.G.M. Medical College and L.S.K. Hospital, Kishanganj.
2. Fifty normal subjects without essential hypertension between the age group of 25-75 years.

Exclusion Criteria

1. Patients with secondary hypertension and complications of Cardiovascular, renal disorders and stroke.
2. History of multiple transfusions, renal disease.
3. Pregnancy, anaemia and history of any other medical or surgical illness.

Control Group

1. Normal volunteers in the age group of 25-75years were screened for same parameters which were done for cases.

Method of Collection of Data

- Blood samples from the study and control group were drawn under full aseptic precautions, after obtaining informed consent.
- Fasting blood sample was collected in Clot Activator and fluoride EDTA vacuum evacuated tubes from both study and control group under full aseptic precautions after obtaining informed consent.

The biochemical parameters were estimated using the following methods

- 25 (OH) vitamin-D by chemiliuminiscence (CLIA)
- Serum Uric acid by enzymatic photometric method by fully automated analyser. (Selectra Pro-M).

The study required investigations to be conducted on patients as mentioned above after obtaining the informed consent from patients. There was no financial liabilities on patients.

Ethical Clearance

Yes, ethical clearance has been obtained from the ethical committee of M.G.M. Medical College and L.S.K. Hospital, Kishanganj.

Plan for analysis

Data entry was done after collection of relevant data (Oral questionnaires and Blood samples) for a given patient was complete. Data analysis was done after completion of data collection from all patients. Data was analyzed for any Mean & ±SD value, significant correlation between the parameters form the data collected. Statistical Package for Social Science software (SPSS-IBM ver 26)was used for data analysis.

ISSN(O):2687-5365; ISSN(P): 2753-6556

RESULTS

Table 1: Age Distribution among case & Control group

Age in Years	Case(n=50)		Control(n=50)	
	No	Percentage	No	Percentage
25 – 30	04	08	16	32
31 – 40	06	12	09	18
41 – 50	12	24	15	30
51 – 60	17	34	08	16
61 – 75	11	22	02	04
Total	50	100	50	100
Mean& SD Value	52.960±11.67		41.940±12.54	
p-Value	0.407			

Table 1 shows the age distribution of both case and control group. In case group 51-60 years and in control group 41-50 years was the commonest age group involving 34% and 30% patients respectively. The mean age in case and control was 52.96 years and 41.94 years respectively with no significant difference between two groups (p value =0.407).

Table 2: Distribution of Age & Sex among case & Control group

Age in Years	Case(n=50)				Control(n=50)			
	Male	%	Female	%	Male	%	Female	%
25 – 30	03	06	01	02	09	18	07	14
31 – 40	04	08	02	04	05	10	04	08
41 – 50	08	16	04	08	10	20	05	10
51 – 60	09	18	08	16	06	12	02	04
61 – 75	01	02	02	04	01	02	01	02
Total	33	66	17	34	31	62	19	38

Age and sex distribution of the study participants is mentioned in Table 2. In our study majority of the study subjects were male in both case and control group involving 66% of case and 62% of control group respectively.

Table 3: Mean & SD Value of systolic blood pressure according to Hypertension stage among Case Group

Hypertensive stage	Mean	SD
Pre- Hypertension	133.33	±2.58
Stage-I	150.720	±6.31
Stage-II	171.789	±8.99

The mean systolic blood pressure level of patents in case group according to the stage of hypertension is mentioned in Table 5. The mean systolic blood pressure in pre-hypertension, stage I and stage II was 133.33±2.58 mmHg, 150.720±6.31 mmHg and 171.789±8.99 mmHg respectively.

Table 4: Mean and SD value of SBP & DBP among Case & Control Group

Blood Pressure (mmHg)	Case(n=50)		Control(n=50)		p Value
	Mean	SD	Mean	SD	
SBP	156.640	±14.94	114.740	±3.22	<0.001
DBP	92.340	±9.75	71.400	±4.04	<0.001

Table 4 shows the comparison of mean SBP and DBP between case and control group. The mean SBP level in case and control group was 156.640±14.94 mmHg and 114.740±3.22 mmHg respectively with statistically significant difference (p value <0.001). The mean DBP level in case and control group was 92.340±9.75mmHg and 71.400±4.04 mmHg respectively with statistically significant difference (p value <0.001).

Table 5: Mean & SD Value of Uric acid and Vitamin-D among Case & Control group

Uric Acid & Vitamin-D	Case(n=50)		Control(n=50)		p Value
	Mean	SD	Mean	SD	
Uric Acid	6.570	±0.79	4.610	±0.51	0.04
Vitamin-D	23.140	±5.39	43.360	±13.59	<0.001

Table 5 shows the comparison of serum uric acid and Vitamin D level between case and control group. Inference: Uric acid was significantly increased Vitamin-D level was significantly decreased in case group compared to control (p value= 0.04 and <0.001 respectively).

ISSN(O):2687-5365; ISSN(P): 2753-6556

Table 6: Correlation between Vitamin–D vs Systolic Blood Pressure in case group

Correlations (Vitamin-D vs SBP)			
		Vitamin-D	**SBP**
Vitamin-D	Pearson Correlation	1	-.712**
	P Value		.000
	No of cases	50	50
**. Correlation is significant at the 0.01 level (2-tailed).			

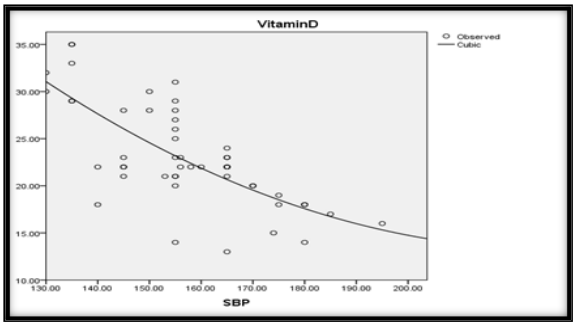

Figure 6: Correlation between Vitamin –D vs Systolic Blood Pressure

Table 6 shows the correlation between Vitamin D level and Systolic blood pressure in case group. Inference: That showed, SerumVitamin-D level is negatively correlated with Systolic blood pressure. R-value was -0.712 and p value <0.001.

Table 7: Correlation between Vitamin –D vs Diastolic Blood Pressure in case group

Correlation between Vitamin –D vs DBP			
		Vitamin-D	**DBP**
Vitamin-D	Pearson Correlation	1	-.588**
	p. Value		.000
	No of cases	50	50
**. Correlation is significant at the 0.01 level (2-tailed).			

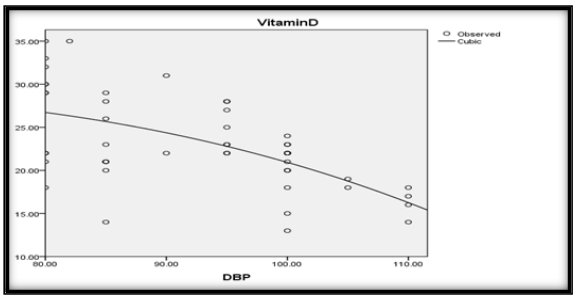

Figure 7: Correlation between Vitamin –D vs Diastolic Blood Pressure in case group

Table 7 shows the correlation between Vitamin D level and Diastolic blood pressure in case group. Inference: That shows a strong negative correlation of serum Vitamin-D level with Diastolic blood pressure. R-value is -0.588 and p value is <0.001.

Table 8: Correlation between Uric Acid vs Systolic Blood Pressure in case group

Correlation between Uric Acid vs SBP			
		SBP	**Uricacid**
SBP	Pearson Correlation	1	.905**
	p Value		.000
	No of cases	50	50
**. Correlation is significant at the 0.01 level (2-tailed).			

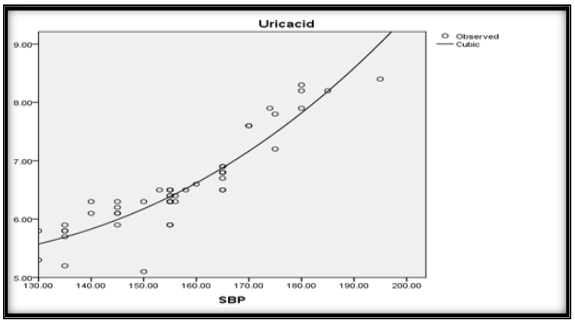

Figure 8: Correlation between Uric Acid vs Systolic Blood Pressure in case group

Table 8 shows the correlation between serum uric acid level and Systolic blood pressure in case group. Inference: That indicates a Positive correlation of Uric acid to Systolic blood pressure. R value was 0.905 and p value was <0.001.

Table 9: Correlation between Uric Acid vs Diastolic Blood Pressure in case group

Correlation between Uric Acid vs DBP			
		Uricacid	**DBP**
Uric acid	Pearson Correlation	1	.856**
	p Value		.000
	No of cases	50	50
**. Correlation is significant at the 0.01 level (2-tailed).			

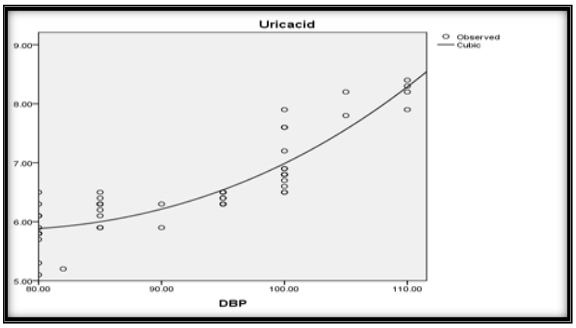

Figure 9: Correlation between Uric Acid vs Diastolic Blood Pressure in case group

Table 9 shows the correlation between serum uric acid level and Diastolic blood pressure in case group. Inference: It indicates that Uric acid is positively correlated with Diastolic blood pressure. R value was 0.856 and p value was <0.001.

DISCUSSION

In the present study the mean age of patients in hypertension group and control group was 52.960 + 11.67 years and 41.940+ 12.54 years respectively. We observed there is an increase in the age of hypertension group, however the difference was not

ISSN(O):2687-5365; ISSN(P): 2753-6556

statistically significant. The results of our study are similar to the study done by Padalkar RK et al.[8] who studied the Impact of Serum Uric Acid and Vitamin D on Essential Hypertension. Kar A and DattaS.[9] in their study of serum Vitamin D level and its association with hypertension reported mean age of hypertensive patients and controls to be 53.24 years and 46.75 years. Divyen K et al.[10] in their Study of Evaluation of Role of Serum Uric Acid Levels in Cases ofEssential Hypertension reported mean age of hypertensive patients and controls to be 54.6 years and 49.6 years respectively. Both the studies reported increased mean age in case of hypertensive patients as compared to controls. The male to female ratio in hypertension group is 1.941:1 and male to female ratio in control group is 1.631:1. Males were significantly more in number as compared to females in both the groups. The findings of our study are concordant with the study done by Padalkar RK et al.[8]Kar A and Datta S.[9] and Divyen K et al.[10] who also reported increase in number of male patients as compared to females. In the present study the mean serum Vitamin D level of patients in hypertension group and control group is 23.140+5.39 ng/mL and 43.360+13.59 ng/mL respectively. Mean serum Vitamin D level of hypertension group is significantly lower than the control group. The results of our study are in concordance with the studies done by Padalkar RK et al.[8]Kar A and Datta S.[9] and Vatakencherry RJ and Saraswathy L.[11]who reported decreased levels of Vitamin D in hypertension group. Vitamin D plays a key role in parameters that regulate high blood pressure via proliferation of vascular smooth muscle cells, endothelial cell function, regulation of renin angiotensin aldosterone pathway, and in regulation of blood pressure via increased intracellular calcium leading to decreased renin activity.[11] There are studies which showed widespread prevalence of Vitamin D deficiency in India.[12] Poor sun exposure due to modern lifestyle, vegetarian diet, skin pigmentation, and cultural practices may be the reasons for this high prevalence in our population. Vitamin D is synthesized when the UV rays from the sun fall on the skin. Till recently, it was believed that Indians had sufficient amount of Vitamin D. Since Indians are now confined to more indoor jobs, and thus less sun exposure, most of us are now Vitamin D deficient. Absence of sunlight hits production of vitamin D in the body, adversely affecting blood pressure. Salt intake, smoking, obesity and genetics are now considered as the contributors for hypertension. In the coming years, Vitamin D deficiency may be included as a contributor for hypertension.[11] Elevated serum uric acid levels have been associated with an increased risk for cardiovascular disease. The potential mechanisms by which serum uric acid may directly affect cardiovascular risk include enhanced platelet aggregation and inflammatory activation of the endothelium.[13]In few studies, the association of serum uric acid with cardiovascular disease was uncertain after multivariate adjustment as in the Framingham Heart Study 10 and the ARIC study , but in others such as the study done by verdecchia et al.[14] the association remained certain and significant. In the study of Breckenridge.[5] excretion of uric acid and uric acid clearance were lower in all hypertensive patients than in the normal group. When the uric acid clearance was expressed per 100ml of glomerular filtrate, there was no significant difference between normal subjects and hypertensive patients who had normal serum uric acid levels, but the difference between those 2 groups and the hyperuricemic hypertensive was significant and they suggested a renal tubular abnormality in the handling of uric acid, the nature of the abnormality which was not clear. Later Messerli et al showed that hyperuricemia in hypertensive is due to early renal vascular involvement, namely nephrosclerosis.[136] Serum uric acid rises because of impaired renal tubular function, which is the main site of regulation of serum uric acid due to nephrosclerosis. Tykarski in his study showed that serum uric acid levels in hypertensives are due to impaired tubular secretion of urate.[15] In the present study incidence and severity of elevated serum uric acid levels between cases and controls correlated significantly with the severity of hypertension. This correlated with both the Kinsey.[16] and Breckenridge.[5] studies, but according to Cannon et al.[17] severity of hypertension had no relation to serum uric acid levels. Our study agrees with the study of Tykarskiet al.[15] in that there is a positive correlation between serum uric acid and severity of hypertension as per the stages but it is not of a linear correlation. Breckenridge.[12] in his study showed an increasing incidence of hyperuricemia as the diastolic BP increased in his study, but there was no tendency for hyperuricemia to occur, only with patients with more severe hypertension.

Hence the possibility of serum uric acid acting by the production of free radicals and causing oxidative stress leading to hypertension and whether the duration and severity of hypertension lead to renal dysfunction in the form of nephrosclerosis leading to higher levels of serum uric acid has to be considered as various other studies have also shown to have a positive relation in the serum uric acid levels and hypertension

CONCLUSION

Serum uric acid is significantly elevated in hypertensive as compared to normotensive individuals. Serum uric acid can be used probably as an early biochemical marker to determine the severity of hypertension as stage 2 hypertensive had more elevation in serum uric acid levels as compared to other hypertensive. Thus serum uric acid estimation can be used for aiding in the

ISSN(O):2687-5365; ISSN(P): 2753-6556

diagnosis of essential hypertension as well as in assessment of the severity. Vitamin D deficiency may be included as a contributor for hypertension. It is not clear whether the changes in uric acid and Vitamin D in essential hypertension is the cause or effect of the disease. But there might be a vicious cycle in the process with the disease. So, it is advisable for all cases of essential hypertension to have routine check up of serum uric acid and Vitamin D and treat the condition along with usual treatment of hypertension.

REFERENCES

1. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. N Engl J Med 2008; 359:1811–1821.
2. Zöllner N. Purine and pyrimidine metabolism. ProcNutrSoc 1982; 41:329–342.
3. Pritsos CA. Cellular distribution, metabolism and regulation of the xanthine oxidoreductase enzyme system. ChemBiol Interact 2000; 129:195–208.
4. Becker BF. Towards the physiological function of uric acid. Free RadicBiol Med 1993; 14:615–631.
5. A. Breckenridge “Hypertension and Hyperuricemia” The Lancet 1966: 287; 15-18.
6. Lu wang. Vitamin and Hypertension. N A J Med. Sci. 2009; 2(4):115-149.
7. Rostand SG. Ultraviolet light may contribute to geographic and racial blood pressure differences. Hypertension. 1997;30:150–6.
8. Padalkar RK, Patil SM, Bhagat SS, Rahul A. Ghone RA, Andure DV The Impact of Serum Uric Acid and Vitamin D on Essential Hypertension. Journal of Practical Biochemistry and Biophysics. 2016;1(1);35-39.
9. Kar A, Datta S. A study of serum Vitamin D level and its association with hypertension. Journal of family medicine and primary care. 2018;7(3):546.
10. Divyen K, Aundhakar SC, SutariyaNirav L, Vartika R, Hardik P. Evaluation of rol of serum uric acid levels in cases of essential hypertension. International Journal of Contemporary Medical Research 2018;5(5):E18-E21.
11. Vatakencherry RJ, Saraswathy L. Association between vitamin D and hypertension in people coming for health check up to a tertiary care centre in South India. J Family Med Prim Care 2019;8:2061-7.
12. Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D. Vitamin D status in Andhra Pradesh: a population based study. Indian Journal of Medical Research. 2008;127(3):211-8.
13. “Systemic Hypertension: Mechanism and Diagnosis.” Elsevier Saunders 37:962.
14. Paolo Verdecchia; Giuseppe Schillaci; GianPaoloReboldi; et al. “Relation Between Serum Uric Acid and Risk of Cardiovascular Disease in Essential Hypertension: The PIUMA Study ”Hypertension. 2000; 36:1072.
15. Tykarski A. “Evaluation of renal handling of uric acid in essential hypertension; hyperuricemia related to decreased urate secretion” Nephrology 1991, 59(3); 364-368
16. Kinsey D., Walther R., Wise HS and Smithwick R. “Incidence of hyperuricemia in 400 hypertensive patients” Circulation, 1961, 24:972.
17. Canon P.J., Stason W.B., Demartini F.E., et al. “ Hyperuricemia in primary and renal hypertension” New England Journal of Medicine 1966;275:457-464.

ISSN(O):2687-5365; ISSN(P): 2753-6556