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## **ASSOCIATION BETWEEN THE HYPERURICEMIA WITH DIABETES AND HYPERTENSION: A HOSPITAL BASED CROSS SECTIONAL STUDY**

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### **ABSTRACT**

**Background:** Diabetes mellitus (DM) and Hypertension (HTN) are most common Non-communicable diseases (NCD). NCDs are the major contributor for morbidity and mortality. To find the relation between the hyperuricemia with diabetes and/or HTN. To know whether treating the hyperuricemia in those patients is significant to prevent complications. **Aim:** To find out what percentage of diabetic / hypertensive patients presenting to our hospital were associated with hyperuricemia and to observe whether hyperuricemia is more significantly related with the hypertension than diabetes among the patients visiting our hospital for treatment. **Materials and methods:** A total of 200 patients visiting our hospital in Department of MHC, Diabetic OPD, and Medicine OPD were selected by convenient sampling and their blood pressure and glucose level along with uric acid level was analyzed. **Result:** The average level of uric acid among the hypertensive patients was  $6.22 \pm 2.06$  mg/dl, which is relatively high whereas the average level of uric acid in patients suffering from both diabetes and hypertension was  $5.23 \pm 1.97$  mg/dl. The average level of uric acid in patients suffering from diabetes was  $4.48 \pm 1.73$  mg/dl, which is near the normal range. Hence the relation between the hypertension and hyperuricemia is found to be significantly higher and a trial of treating hyperuricemia in hypertensive patients may provide better control of hypertension and will help to prevent its complications. Patients with DM do not have significant increase in uric acid level, so hyperuricemia is not significant in DM patients. **Conclusion:** The uric acid level is significantly raised in patients suffering from hypertension and hence early measures has to be taken to reduce the level of uric acid which may play a vital role in control of hypertension at early stages and to prevent hyperuricemia induced diseases like gouty arthritis/ Renal impairment. The uric acid level is insignificant in correlation with diabetes as the mean level is maintained by  $4.48 \pm 1.73$  mg/dl in diabetic patients which is relatively near the normal range.

**Keywords:** Uric acid, Hyperuricemia, Hospital Based Study, Antihypertensive, Diabetes Mellitus (DM), Systemic Hypertension (S.HTN), Non communicable disease (NCD), Master Health Check-up (MHC), Hyperuricemia

### **INTRODUCTION**

Hypertension is a condition in which arterial BP is chronically elevated. Many factors may contribute to the development of hypertension. Renal dysfunction (Kuroczycka Saniutycz *et al.*, 2013) (Zhou *et al.*, 2006), peripheral resistance, vessel tone, endothelial dysfunction, autonomic tone, insulin resistance and neurohumoral factors have significant role in hypertension (Corry *et al.*, 2008, Higashi *et al.*, 2012; and Kang *et al.*, 2005). High salt diet, heavy alcohol consumption, obesity, lack of exercise and impaired intrauterine growth are all the environmental factors which contribute to the development of hypertension (Colledge *et al.*, 2010).

In India, NCDs were responsible for 53 per cent of deaths and 44 percentage of disability adjusted life years lost (Reddy and Shah *et al.*, 2005). HTN and DM remains to be the global threat till date which warrants more and more clinical knowledge about the disease so as to open gates for the researchers on

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different interventions that could control the disease in various ways and in earlier stage (Fuchs Sc *et al.*, 2018). The burden of resistant HTN is highest in patients with chronic kidney disease. New treatments for resistant hypertension are highly needed, considering the disastrous complications of the disease (Noubiap *et al.*, 2019), such as hypertensive retinopathy, renal dysfunction, cerebral stroke and cardiovascular complications. In recent years, the spectrum of interventions to increase hypertension control and reduce cardiovascular risk factors is widening to reduce overburdening the public health system, even with use of technologies using mobile phones and the internet to implement interventions that could improve BP control, minimize health care resource use and costs (Omboni *et al.*, 2013), and reduce cardiovascular risk (Piette *et al.*, 2015) (Cochrane Database of Systemic Review). Effectiveness of these technological approaches depends on patient adherence to both types of interventions—behavioral and pharmacological. Several randomized controlled trials (RCTs) have evaluated also nonpharmacological interventions to reduce BP and, in some studies, stimuli for lifestyle changes (Eisen *et al.*, 2013; Mckinstry *et al.*, 2013; Ralston *et al.*, 2014).

Diabetes is an important cause of disability and death around the world and is a major risk factor for other diseases. The World Health Organization Eastern Mediterranean Region (EMR) has the highest age-standardized rate of disability-adjusted life years (DALYs) from diabetes (Mokdad *et al.*, 2018). Various studies have already been done regarding the relation between the Serum uric acid level and the HTN (Garrick *et al.*, 2008) which showed significant relation of HTN with the elevated serum uric acid level and studies also signified it acted as a vicious cycle in which the elevation of the one component related to the elevation of the other due to relation of the uric acid level with the renin angiotensin system, glomerular apparatus and vascular smooth muscle cell proliferation. If the relation between the hypertension and uric acid is strongly proved it can be tried in the treatment of resistant hypertension patients and even in essential and secondary hypertensive patients for effective control of Bp. The study also tries to find whether the correlation between the DM and hyperuricemia is as significant as in the hypertensive patients by including the people those who have diabetes mellitus and those who have both diabetes mellitus and hypertension. Since most of the diabetic patients are also suffering from HTN (Allcock DM *et al.*, 2010) it's better to find the relation between the uric acid and DM to plan the treatment in a better way in the future.

## **MATERIALS AND METHODS**

**Study Design:** Hospital based cross sectional study

**Study setting:** Out Patient Departments in the MGMCRI Medicine OPD, Diabetic clinic and Master Health Checkup OPD.

**Study Population:** People who were more than 18 years visiting the above mentioned OPDs.

**Inclusion Criteria:** Age between 18 years to 85 years with diabetes mellitus or/and hypertension were enrolled as study group.

**Exclusion Criteria:** Age: Patients with <18 years, Gout, Leukemia, polycythemia, lymphoma, carcinoma, anticancer therapy, psoriasis, pregnancy, chronic disease which causes tissue break down were excluded from the study.

**Study Period:** December 2017 to February 2018.

**Operational definition:** A systolic blood pressure of  $\geq 140$  mm Hg and /or a diastolic blood pressure of  $\geq 90$  mm Hg measured on two separate occasions with a minimum interval of at least five minutes between the two measurements or a self-reported history of taking antihypertensive medications, is defined as hypertension. Diabetes mellitus was diagnosed by measuring random or fasting venous blood glucose. Diagnosis confirmed by Fasting plasma glucose  $>7.0$  mmol/L (126 mg/dL) Random plasma glucose  $>10.1$  mmol/L (140 mg/dL)

**Survey Instrument:** Questionnaire (Structured, pretested)

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### **Logistic Requirements:** Non-Mercury LED Sphygmomanometer

**Sample Size:** Convenience sampling is followed in this study. A convenient sample of 200 is taken.

**Methodology:** The study is a hospital based cross-sectional study carried out in the patients visiting the Medicine OPD, Diabetic clinic and the Master health check-up of MGMC&RI, Pillayarkuppam, Puducherry, which is situated in the Union territory of Puducherry which provides health care services to the people of Puducherry and people of Tamilnadu districts nearby Puducherry (Wright *et al.*, 2001). Convenient sampling is followed in this study. The study data is collected from the people of Puducherry and Tamilnadu with NCD (*i.e.*, either or both DM and HTN) those who come to the Medicine OPD, Master health checkup and to the Diabetic clinic. People were not encouraged to undergo any blood tests for the sake of the study since diabetic and hypertensive patients those who visited the above mentioned OPDs for Physician consultation with blood reports were enrolled in the study after written consent. Complete history and medical examination was done before taking the blood pressure. Blood pressure was measured by mercury free LED BP apparatus after adequate rest to the patient. HTN was defined by blood pressure  $\geq 140/90$ mmhg. Diabetes mellitus was defined by blood sugar level more than 126mg/dl during fasting and more than 140mg/dl in the postprandial. Both diabetic and hypertensive patients those who were previously taking medication were also enrolled in the study despite of normal blood pressure and controlled blood sugar level. The cut off for the normal uric acid is taken as 4.7mg/dl for male and 4.03mg/dl for female ( Poudel *et al.*, 2014).

### **Statistical analysis:**

Data were entered in Microsoft excel spreadsheet. Descriptive statistics like mean, median and proportions were calculated using Stata version 11.

## RESULTS

A total of 200 patients were included in the study. Mean age of study participant was 52 years (SD  $\pm 11.9$ ). A total of 52 female patients and 148 male patients participated in the study. 77 hypertensive patients, 58 diabetic patients and 65 patients those who have both diabetes and hypertension were enrolled in the study. Out of which 10 patients were newly diagnosed hypertensive patients and 18 patients were newly diagnosed diabetic patients and 3 patients were newly diagnosed to have both hypertension and diabetes and 3 hypertensive patients were newly diagnosed to have diabetes. The average uric acid level of all the female patients were  $5.46 \pm 2.2$  and for male patients it was  $5.38 \pm 1.99$ . The average level of uric acid among the hypertensive patients was  $6.22 \pm 2.06$ mg/dl, whereas the average level of uric acid in both disease group patients was  $5.23 \pm 1.97$  mg/dl. The average level of uric acid in patients suffering from diabetes was  $4.48 \pm 1.73$ mg/dl. The result of the study signifies the relation between the hyperuricemia and hypertension. It also signifies diabetes is not related with the hyperuricemia among the patients enrolled in the study. Since the association between the hypertension and the hyperuricemia is significant, further studies with the treatment of hyperuricemia and its effects on the blood pressure of the patient will show a clear picture regarding the initiation of hyperuricemic evaluation and its treatment in the general population.

## DISCUSSION

DM and HTN are the diseases which are included among the top five NCDs which cause mortality and morbidity along with sepsis, cancer and pneumonia (Ichiho HM *et al.*, 2013). Coming to our study, a total of 200 patients were included in the study, in which different age group patients were included varying from 28 to 84 years of age and the mean age of the total people included in the study was 52.08. The mean duration of diabetes among the all diabetic patients in our study was 5.9 years and the maximum duration of diabetes was 45 years whereas newly diagnosed diabetic patients were also included in the study. The frequency of patients in each duration group is mentioned in Table no.1.

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**Table No. 1: Total number of patients in each duration group**

Duration	Hypertensive patients			Diabetic patients		
	Freq.	Percent	Cum.	Freq.	Percent	Cum.
<1yr	38	29.92	29.92	40	34.78	34.78
1-5yrs	34	26.77	56.69	31	26.96	61.74
5-10yrs	35	27.56	84.25	28	24.35	86.09
>10yrs	20	15.75	100.00	16	13.91	100.00
Total	127		100.00	115	100.00	

The mean duration of hypertension among the all hypertensive patients in our study was 6.3 years and the maximum duration of hypertension was 40 years and newly diagnosed hypertensive patients were also included in the study. Table.No.1. shows the detailed view on the duration of hypertension among the study population.

The total study population was categorized into three groups hypertensive patients group, diabetic patients group and both disease patients group (patients having both DM and HTN).

The average level of uric acid among the hypertensive patients was  $6.22 \pm 2.06$ mg/dl and the lowest level of uric acid recorded among the hypertensive patient was 2.3mg/dl and the highest value was 11.4mg/dl.

The average level of uric acid in patients suffering from both diabetes and hypertension was  $5.23 \pm 1.97$  mg/dl and the highest level of uric acid among the both disease group patient was 9.8mg/dl and the lowest recorded was 2mg/dl.

The average level of uric acid in patients suffering from diabetes was  $4.48 \pm 1.73$ mg/dl , the lowest level of the uric acid among the diabetic patient was 2.4 mg/dl and the highest level of uric acid among the diabetic patient was 12mg/dl.

The results shows that there is significant relation between the increased uric acid level and hypertension, since the mean uric acid level is relatively high in hypertensive patients group and both diseases patients group when compared to the diabetic alone patients group. The level of uric acid between diabetic patients group, hypertensive patients group and both disease patients group is found to be statistically significant(p value is 0.000).The level of uric acid among the three groups is found to be statistically significant by one way annova test (p value is 0.000).

**Table No. 2: Comparison of Uric acid(mg/dl) by Disease (Bonferroni)**

Row mean	1	2
Column mean		
2	-0.99011 0.009	
3	-1.74064 0.000	-0.750531 0.102

On coming to comparison within the group, we found that uric acid level variation is statistically significant between hypertensive patients group and both disease patients group(p value is 0.009).The level of uric acid between diabetic patient group and hypertensive patient group(p value 0.000) is also statistically significant. But it was statistically insignificant between diabetic patient group and both disease patient group(p value is 0.102).So these results shows that having diabetes alone doesn't have much effect on the serum uric acid level but having hypertension with or without diabetes significantly affects the serum uric acid level. Our studies result are in the favor of other studies such as the study done in the Nepalese population (Poudel B *et al.*, 2014) which shows the relation between the increased uric

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acid level and the hypertension. The Nepalese studies observed mean level of serum uric acid in hypertension and control were ( $290.05 \pm 87.05 \mu\text{mol/l}$  ( $3.2 \pm 0.98 \text{ mg/dl}$ )) and ( $245.24 \pm 99.38 \mu\text{mol/l}$  ( $2.7 \pm 1.12 \text{ mg/dl}$ )) respectively ( $p < 0.001$ ).

**Table 3: Uric acid different age group**

Age.	No.	Percent.	Avg. uric acid
18-30 yrs	3	1.50	6.933333
31-60 yrs	148	74.00	5.29527
>60 yrs	49	24.50	5.630612
Total	200	100.00	

A total of 3 patient categories in our study, in that 3 patients were from 18 to 30 years category and 148 patients from 31 to 60 years category and 49 patients from >60 years category (Table. No.3) and the mean uric acid level in each age group was found to be  $6.93 \pm 1.45$ ,  $5.29 \pm 2.12$  and  $5.63 \pm 1.89$  respectively. Significant high serum uric acid level in hypertensive patients were also observed by Eisen *et al.*, 2013; and Grayson *et al.*, 2011.

The mean value of systolic blood pressure and diastolic blood pressure in our study hypertensive patients group were  $141.38 \pm 19.15$  and  $87.03 \pm 10.6$  which is relatively lower than the study done in Nepalese population (systolic and diastolic were  $143.99 \pm 14.28$  and  $96.61 \pm 7.24$  respectively) and which was higher than the mean values of systolic blood pressure and diastolic blood pressure in patients of Feig *et al.* (2008) study). Feig *et al.*, (2008) found the mean level of systolic blood pressure and diastolic blood pressure 139 mm hg and 83 mmhg respectively. Our study has shown a significant correlation between the increased uric acid level and the hypertension which is coinciding with the results of other studies (Loeffler *et al.*, 2012; Grayson *et al.*, 2011; Qiu *et al.*, 2103; Yoo *et al.*, 2005). As described in the Yoo study (Yoo *et al.*, 2005) there was significant relation between serum uric acid, hypertension, heart failure and other cerebrovascular and cardiovascular studies which is also supported by the other studies. This signifies the importance of treating the hyperuricemia in patients having hypertension. A unique study done in US (Loeffler *et al.*, 2012) regarding the correlation between the uric acid level and hypertension in adolescent a trial of treatment with allopurinol 300mg/day for 3 months showed a significant decrease in the mean systolic and diastolic pressure by 3.9 and 1.9 mmhg respectively and a clinical trial in children of randomized double blind, placebo controlled, cross over study with treatment of allopurinol showed a significant decrease in the blood pressure when compared to the placebo. There was a limitation in that study (Loeffler *et al.*, 2012) where newly diagnosed hypertensive patients were checked for BP at one sitting (2 measurements on same day) which is a limitation in our study too since we have checked Bp in the OPDs on the patients visiting day only, where newly diagnosed hypertensive were not checked for BP on second day or in follow up days (Loeffler *et al.*, 2012). The study result cannot be exponentially applied to the country or the state due to certain limitations in our study such as convenient sampling and patients medication history was not taken into consideration and it will be better to start treating the hyperuricemia in hypertensive patients after confirming the same result in the different parts of the world in the near future, If the benefit of adding a drug (Pathak *et al.*, 2018; and Ernst *et al.*, 2009) to treat the hyperuricemia is found to be better than the risk of adding one more drug to the patients drug list it can be very well practiced without further delay since the mortality due to noncommunicable diseases are fastly growing now a days due to the lifestyle modification and dietary modification.

### CONCLUSION

This hospital based study has showed a significant relation between hypertension and hyperuricemia. Strategies should be identified to diagnose hypertension at an early stage and prevent or postpone its complications as burden of hypertension is bound to increase due to increasing life expectancy rates. It will also reduce the other ill effects of the hyperuricemia in hypertensive patients. Further studies in the



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hypertensive patients those who were started on drug for hyperuricemia such as Febuxostat(Pathak R K *et al.*, 2018) (Ernst *et al.*, 2009), so as to know the benefits of treating hyperuricemia better.

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