Association of uric acid level among diabetic and hypertensive patients

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Abstract

Objectives: To compare the association and determine whether there is any significant relationship between uric acid level of normal, diabetic, hypertensive and subjects having both diabetes and hypertension.

Methodology: It's a cross sectional study done in our institute. Subjects were taken from both outdoor patients and indoor patient. A total of 214 subject were taken in study out which 56, 50, 51 and 57 were normal, hypertensive, diabetic and both hypertensive as well as diabetic respectively. Subjects were diagnosed as diabetic or hypertensive and the data were collected and analysed.

Observation: There is significant increase in uric acid level in subject with hypertensive, diabetic and diabetic with hypertension i.e., 52 %, 33.3% and 57.89% respectively. The uric acid level in hypertensive patient is future increases if the subject is also having diabetes. Patient with controlled blood pressure and glycaemic level were having uric acid level within the normal range.

Conclusion: Patients with high uric acid level should have a strict blood pressure and blood glucose control. All the hypertensive patients should be screened for uric acid level yearly till 5 years then every half-yearly after 5 year of disease.

Keywords: Diabetes, Hypertension, Uric Acid, Metabolic Syndromes, Glycaemic, Blood Pressure.

Introduction

Uric acid is the end product of purine metabolism generated in liver. Purine nucleotides breakdown to hypoxanthine and guanine, a part of it is recycled and phosphorylated into hypoxanthine nucleotides, while the remaining part is metabolized by xanthine dehydrogenase/ oxidase enzyme to terminal product uric acid [1]. Excesses in production or decrease excretion will lead to hyperuricemia that may lead to gout and urolithiasis [2]. Uric acid is also a risk factor for peripheral arterial disease, insulin resistance and metabolic syndrome and it act as a marker for cardiovascular diseases [3-5]. Uric acid can also be used as a marker of progression to complication of hypertension and diabetes and it has been known that uric acid level itself is a potentially modifiable risk factor of cardiovascular diseases [6-7]. It has been seen that there is linear association between blood glucose and uric acid levels [8]. Serum uric acid is positively linked with serum glucose in healthy subjects [9].

However, this association is not consistent between healthy and diabetic individuals, as a low serum level of uric acid is reported in the hyperglycaemic state [10]. Uric acid act as pro-oxidant and thus can be used as marker of oxidative stress [11]. Data exist that uric acid level is associated with risk factor and complications of diabetes and hypertension [12,13]. Uric acid is also associated with the development of both hypertension and diabetes [14,15,16]. As the prevalence of hypertension and diabetes is increasing day by day due to sedentary life style that we are adopting now a days, which was most common in developed countries but now a days it has become common in developing counties like India. It is estimated that 35% of urban and 25% of rural population may be suffering from either hypertension or diabetes by 2025. The leading cause of cardiovascular disease are hypertension and diabetes mellitus [17,18]. So, it becomes necessary to have a study to evaluate association of uric acid in hypertension and diabetes before it progresses to its complication.

Research design and methods

The Study was done at GCS Medical College, Hospital and Research Centre, Ahmedabad. Written consent was obtained from all participants, and the institutional Medical Ethics Committee has approved the study. A total 214 cases were taken in study, out of which 56, 50, 51 & 57 were normal, hypertensive, diabetics and having both hypertension and diabetes respectively. All the subjects belong to middle- and low-income group. The inclusion criteria for selection of cases were subjects of age > 30 years and duration of illness more than 5 years, it may be either hypertension or diabetes or both hypertension and diabetes. Normal subject included were not suffering from hypertension and diabetes. Study subjects were selected randomly from outpatient department and indoor patients. Subjects

suffering from any other metabolic diseases like gout, duration of illness < 5 years, type 1 diabetes mellitus, secondary hypertension or with any microvascular and macrovascular complications of diabetes and hypertension were excluded from the study. Renal involvement was assessed by calculating eGFR and serum creatinine level, neurological assessment was done by doing NCV, retinopathy by doing fundus of selected patients and cardiac vascular system assessment by doing electrocardiogram, 2-dimensional echocardiography and renal doppler. Uric acid levels were seen in all the subjects taken in study and with the reference level of 4.5-6 mg/dl as per gradation of institute laboratory readings were considered and subjects were sorted. The association was assessed by Cox regression analysis. The population-attributable risk and 95% CIs were calculated with use of the Interactive Risk Assessment Program (IRAP). The subjects were divided into four quartiles (quartile 1 includes normal subject, similarly quartile 2, 3 and 4 includes hypertensive, diabetes and hypertensive with diabetes).

Diabetes was diagnosed as per American Diabetes Association Guideline

Guidelines for diagnosis of DM-2

1. Symptoms of diabetes such as polydipsia, polyphagia, polyuria plus RBS ≥ 200mg/dl or,
2. FBS ≥ 126mg/dl or,
3. HbA1c ≥ 6.5 % or,
4. 2hr plasma glucose ≥ 200mg/dl during an oral glucose tolerance test.

(Random is defined as sugar level at any time of the day and Fasting is defined as no calorie intake for at least 8 hrs.)

And hypertension was classified according to JNC VII

Sn.	Classification of BP	SBP (mmHg)	DBP (mmHg)
1	Normal	≤ 120	≤ 80
2	Pre-Hypertension	120-139	or 80-89
3	Stage 1 HTN	140-159	or 90-99
4	Stage 2 HTN	≥ 160	or ≥ 100

SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure

(Preparation of subjects prior to blood pressure measurement were

1. Subjects were asked to sit calm for 15 - 30 minutes
2. Shouldn't have taken tea or coffee or smoked within 1 hour
3. Both the arms blood pressure were measured and higher reading was considered)

Observations

A total 214 subject were taken into study, most of the patient were of age group 50-60. Out of which females subjects were 126 (62.15%) (Table 1, Figure 1) and sex distribution ratio was approx. M: F = 3:5. It was observed that the incidence of hypertension and diabetes were more common in females than in males below 60 years of age and after 60 years it becomes equal or reversed in ratio, these may be due to sedentary life style of females in comparison to males. Less number of patients were above 60 years, may be due to decrease in life expectancy of patients due to co-morbidity. Young subjects in the age group 30-40 years were having a family history of hypertension or/and diabetes.
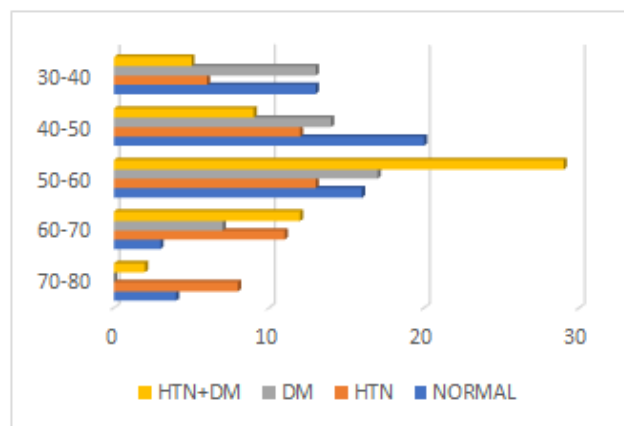

Fig. 1: Age wise distribution of selected cases

sex → Age (in yrs) ↓	Normal MALE	Normal FEMALE	HTN MALE	HTN FEMALE	DM MALE	DM FEMALE	HTN+DM MALE	HTN+DM FEMALE	Total
	4		8		0		2		14
70-80	3	1	6	2	0	0	1	1	
	3		11		7		12		33
60-70	2	1	5	6	4	3	6	6	
	16		13		17		29		75
50-60	8	8	3	10	6	11	13	16	
	20		12		14		9		55
40-50	5	15	3	9	2	12	3	6	
	13		6		13		5		37
30-40	5	8	4	2	5	8	1	4	

Table 1: Age and sex wise distribution of selected cases

Quartiles	Groups ↓	No. of patient	CL (95%)	RANGE	SD	p-value
Quartile 1	Normal	56	0.39	5.55-4.78	1.5	-
Quartile 2	Hypertension	50	0.47	6.54-5.61	1.65	0.0035
Quartile 3	Diabetes	51	0.63	6.46-5.19	2.25	0.05
Quartile 4	Hypertension + diabetes	57	0.47	6.46-5.53	1.75	0.0072

CL-confidence level; SD- standard deviation

Table 2: Statistical analysis of subject taken in study

The p-value of hypertension, diabetes and hypertension with diabetes was calculated by unpaired two tailed student 't' test and pearson's coefficient, in comparison to normal subject that is < 0.05 which implies that there is a significant relationship between the quartiles. The odd ratio confidence levels (95%) was calculated (Table 2). It was observed that among 214 subjects, 41.12% of subject i.e., 88 patients were having high uric acid level and subject with high uric acid in normal, hypertension, diabetes and with both

hypertension and diabetes subjects were 5.61%, 12.15%, 7.94% and 15.42 % respectively (Table 3). And among hypertensive, diabetics and hypertensive with diabetic 52%, 33.33% and 57.89% respectively were having high uric acid level. Females in all the four quartiles were having increased uric acid level (Table 3). Chi-square value was calculated which is 17.27 and p-value was deduced from it that was 0.0006; that suggest there is significant correlation between the levels of uric acid in normal, hypertension, diabetes and diabetes with hypertension (Table 3). Cramer's V was also calculated i.e., 0.28. Increased uric acid level was significantly more in subjects with hypertension.

Uric acid level	NORMAL	HTN	DM	HTN+DM	Total	Chi-square value	Chi-Square P-value	Cramer's V
>/=6	12	26	17	33	88	17.273		
<6	44	24	34	24	126		0.0006	0.28410377
Total	56	50	51	57	214			

Table 3: Uric acid levels observed

Subject with high uric acid levels were again categorised according to sex. 48.8% (40 subject) of patients were females. More hypertensive male were having increased uric acid where as in diabetic subject more females were having increased uric acid level (Table 4). Chi-square value was calculated and p-valve was 0.036 which also suggest there is significant relationship between the groups (Table 4). Cramer's V was also calculated which is 0.2. 55.14 % of patient with hypertension were having increased level of uric acid. Whereas 46.3 % of diabetic patient were having increased uric acid. Out of 88 subject with high uric acid 42.31%, 70.59% and 54.55% were females with hypertensive, diabetes and hypertensive with diabetes respectively.

group → gender↓	NORMAL	HTN	DM	HTN+DM	Total	Chi-square value	Chi-Square P-value	Cramer's V
FEMALE	2	11	12	18	43	8.596		0.200420
MALE	10	15	5	15	45		0.0351	12
Total	12	26	15	30	88			

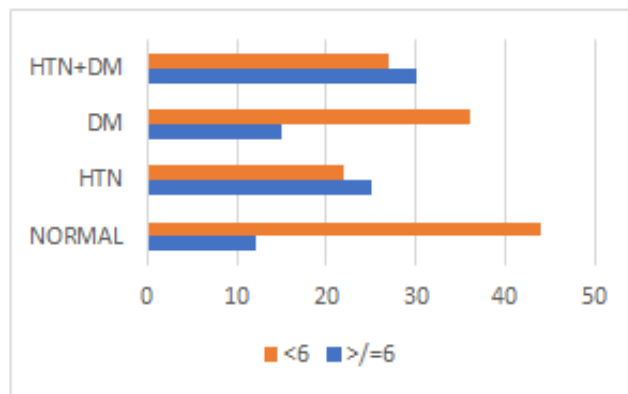Table 4: Sex distribution seen in patient with high uric acid level
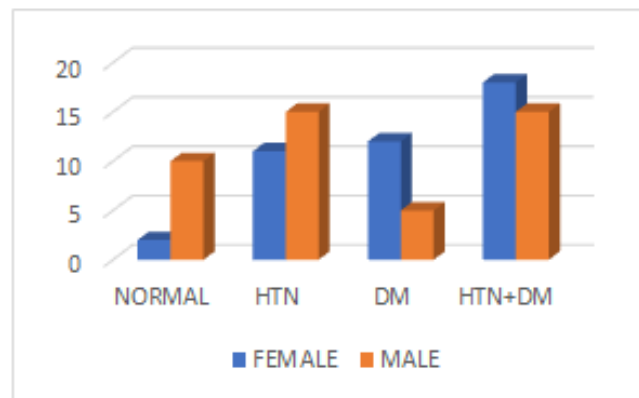

Fig. 3: observation of uric acid level

Fig. 4: Sex distribution seen in patient with high uric acid level

Discussions

Type 2 diabetes mellitus and hypertension are two important public health challenges, and both are linked to increased risk of cardiovascular events. Hyperuricemia has recently emerged as an independent risk factor in the development of type 2 diabetes mellitus and hypertension through several proposed mechanisms. Few clinical trials investigated the use of uric acid lowering agents in the management of these two disease entities; however, their results provided

encouraging evidence to a potential role for these agents in fighting disease burden. Larger randomized controlled trials are therefore warranted to establish the role of uric acid as a promising target for novel therapeutic interventions in the management of type 2 diabetes mellitus and hypertension. Every patient with hypertensive and diabetes should be screened for it to avoid complications leading to cardiovascular diseases. Good blood pressure control and glycaemic control is required to have a uric acid level low. Thus, it is evident that uric acid is an important biomarker of cardiovascular disease so every patient with hypertension and diabetes should be screened for it to avoid complications leading to cardiovascular diseases.

Abbreviations

HTN – Hypertension

DM – Diabetes mellitus

RBS – Random blood sugar

FBS – Fasting blood sugar

SUA – Serum uric acid

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