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Original Research Article

CORRELATION OF SERUM URIC ACID LEVELS WITH HbA1C IN TYPE 2 DIABETES MELLITUS WITH AND WITHOUT HYPERTENSION

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ABSTRACT

Background: DM and Hypertension are interlinked diseases, which are the risk factors, alone or combined, predispose an individual to atherosclerotic cardiovascular disease. Primary hypertension is associated with hyperuricemia as well as tends to be more common with accelerated (or malignant) hypertension. An increased serum uric acid is likewise one of the predictors of diabetes and normally precedes the improvement of each insulin resistance and diabetes. **Objective:** To estimate the serum uric acid levels in type 2 diabetes mellitus with and without hypertension and to correlate serum uric acid levels with the glycated haemoglobin in type 2 diabetes mellitus with and without hypertension.

Materials and Methods: This Cross-Sectional study had been done over a period of 18 months from 1st August 2022 to 31st January 2024 on 150 patients attending Department of General Medicine at KBN Teaching and General Hospital, Kalaburagi on both outpatients and inpatients. The patients were grouped into group A which included 75 T2 DM patients with Hypertension and group B which included 75 T2 DM patients without Hypertension.

Result: The mean uric acid levels of group A was 6.66±1.72 and of group B was 5.62±1.51 which was statistically highly significant (t = 3.915, p= <0.001). In group A, among females 0 (0%) had low,16 (43.2%) had normal and 21 (56.8%) high uric acid levels, among males 0 (0%) had low, 16 (42.1%) had normal and 22 (57.9%) high uric acid levels. In group B, among females 0 (0%) had low, 26 (60.46%) had normal and 17 (39.5%) high uric acid levels, among males 1 (3.1%) had low, 26 (81.3%) had normal and 5 (15.6%) high uric acid levels. Even though both groups had elevated mean uric acid levels, group A had very significant elevation than group B (t= 2.521, *p*= <0.001). The mean HbA1C level in group A was 9.92±2.16 and in group B was 9.04±2.10 which was statistically significant (t = 2.521, P = 0.013). The mean serum uric acid level increased with increase in HbA1C levels in both the groups, but the correlation with group A was statistically very significant (r = +0.313, p < 0.01) compared to group B (r = +0.291, p< 0.05).

Conclusion: T2 DM with hypertension are more prone to develop hyperuricemia than without hypertension. SUA is linearly and positively associated with increase in levels of HbA1C in both the groups. Hence it is sensible to monitor serum uric acid levels, HbA1C levels and blood pressure in Type 2 Diabetes mellitus with or without hypertension, to prevent morbidity and mortality due to diabetic complications.

Keywords: Serum uric acid, HbA1c, Diabetes Mellitus, Hypertension.

INTRODUCTION

DM and Hypertension (HTN) are interrelated diseases that strongly predispose an individual to atherosclerotic cardiovascular disease (CVD). According to the data obtained from death certificates the hypertension has been implicated around 4.4% of deaths coded to diabetes, whereas, diabetes was involved in 10% of deaths coded to hypertensive disease.[1]

Epidemiological research has documented that insulin resistance and diabetes now not only simplest represent metabolic abnormalities but additionally predisposes to hypertension, vascular stiffness, and related cardiovascular disease and in-turn excessive arterial stiffness and impaired vasorelaxation worsens the insulin resistance and the development of diabetes. Inappropriate activation of the renin-angiotensin-aldosterone system and sympathetic nervous system, mitochondria dysfunction, excessive oxidative stress, and systemic inflammation were proposed molecular mechanisms promoting hypertension in diabetes.[2]

A common comorbidity in patients with type 2 diabetes is hypertension. Compared with general population the prevalence of hypertension is higher in patients with diabetes. Approximately 74% of adult patients with diabetes have a blood pressure ≥140/90 mmHg or are on prescription medication for high blood pressure.[3]

Two important public health challenges which are interlinked to increase the risk of cardiovascular events, are diabetes mellitus and hypertension. One of the risk factors, which emerged recently as an independent risk factor in the development of type 2 diabetes mellitus and hypertension through several proposed mechanisms, is hyperuricemia (HUA). Gout, most common inflammatory arthritis characterized by painful disabling acute attacks, is known to be caused by HUA. However, recent evidence suggests an emerging association between HUA, hypertension, and type 2 diabetes mellitus.[4]

Hyperuricemia is incredibly prevalent, affecting about 38 million people withinside the United States. However, the significance of asymptomatic hyperuricemia i.e., hyperuricemia in the absence of gout – is still a debatable topic. The effect of asymptomatic hyperuricemia is that the deposition of monosodium urate crystal in tissues worsens chronic inflammation. Intracellularly, hyperuricemia inhibits the grasp regulator adenosine monophosphate (AMP)-related protein kinase and can circumstance innate immune responses via long lasting epigenetic modifications. At the populace level, asymptomatic hyperuricemia is related to a couple of comorbidities, along with hypertension, persistent kidney disease, coronary artery disease, and diabetes; boundaries of those research consist of that maximum are retrospective and some do not rigorously distinguish between asymptomatic hyperuricemia and gout.[5]

MATERIALS AND METHODS

This Cross-Sectional study has been done over a period of 18 months from 1st August 2022 to 31st January 2024 on 150 patients attending Department of General Medicine at KBN Teaching and General Hospital, Kalaburagi on both outpatients and inpatients. The patients were grouped into group A which included 75 T2 DM patients with Hypertension and group B which included 75 T2 DM patients without Hypertension.

Sample Size: 150

Inclusion Criteria

1. Male and Female patients in the age group of 40-70 years diagnosed with hypertension in type 2 diabetes mellitus.
2. Individuals with normotensive type 2 diabetes mellitus.

Exclusion Criteria

1. Individuals with hypertension only, without Type 2 DM.
2. Individuals diagnosed with MODY.
3. Individuals known to have cardiovascular disease.
4. Individuals who had stroke.
5. Patient with pre-existing renal disease.
6. Patients on drugs which alters serum uric acid levels [thiazides, loop diuretics, pyrazinamide, allopurinol, levodopa, ethambutol, cytotoxic drugs etc.]
7. Patients whom consumes alcohol regularly.
8. Patients on chemotherapy and antimetabolite.
9. Clinical Findings of gout or extra- articular manifestations of Hyperuricemia.

Study subjects were selected after applying inclusion, exclusion criteria. Information was collected through prepared proforma from each case by simple random sampling technique. The serum uric acid levels were estimated by using uricase method. According to that, the patients were classified to have low, normal and high SUA levels if <2.5 mg/dl, 2.5 – 6, >6 mg/dl for females and <3.5, 3.5-7, >7 for males, respectively.

Investigations: FBS, PPBS, HbA1C, Serum Uric Acid

Statistical Data Analysis: Statistical data was analyzed by IBM SPSS 25.0 version software. Collected data were spread on excel sheet and prepared master chart. Through the master chart tables and graphs were constructed. For quantitative data analysis mean and standard deviations were calculated and t-test and correlation tests applied for statistically significant. For qualitative data analysis chi-square test and Fisher exact tests were applied for statistical significance. If P-value was less than 0.05 considered as significant.

RESULTS

In the present study; Out of 150 sample individuals; 75 (50.0%) of patients were DM with HTN (Hypertensive) and 75 (50.0%) of individuals were DM without HTN (Normotensive).

Maximum number of individuals 69 (46.0%) were belongs to the age group of 40—50 years, followed by 46 (30.7%) of individuals were belongs to the age group of 51-60 years and 35 (23.3%) of individuals were belongs to the age group of 61—70 years. Minimum age of the individual was 40 years and maximum age of the individual was 70 years. The mean age of DM with HTN individuals was 52.80 years and the mean age of DM without HTN individuals was 55.25 years. The mean age of all individuals was 54.02 years. There was statistically no significant difference of age among patients of DM with HTN and DM without HTN (P>0.05)

Study observed that; out of 150 individuals, 80 (53.3%) of patients were females and 70 (46.7%) of individuals were males. The sex ratio of male to female was 1:1.14, In the distribution of gender between DM with HTN and DM without HTN groups, showed no significant difference (P>0.05).

Table 1: Comparison of BMI between the individuals of group A and group B

BMI kg/m²	Categories	Group A		Group B		Total	
		No	%	No	%	No	%
< 18.5	Under weight	0	0.0	1	1.3	1	0.7
18.5–24.9	Normal weight	17	22.7	24	32.0	41	27.3
25.0—29.9	Overweight	25	33.3	29	38.7	54	36.0
30—34.9	Obesity	20	26.7	16	21.3	36	24.0
≥ 35	Obesity Class-I	13	17.3	5	6.7	18	12.0
Total	----	75	100.0	75	100.0	150	100.0
Mean ± SD	------	28.90 ± 4.92		27.58 ± 4.32		28.24 ± 4.61	
P-value	t = 1.750 P = 0.082, NS						

In the study, majority of individuals 54 (36.0%) were overweight, followed by 41 (27.3%) of individuals were normal weight and 36 (24.0%) and 18 (12.0%) of individuals were obese and obesity class-I respectively. The mean BMI score in DM with HTN was 28.90 and the mean BMI score in DM without HTN was 27.58, which was statistically insignificant (P>0.005).

Table 2: Comparison of FBS and PPBS between the individuals of group A and group B

Variables	Group A	Group B	t-test value, P-value & significance
	Mean ± SD	Mean ± SD	
FBS	192.62 ± 72.32	180.80 ± 56.60	t = 1.115, P = 0.267, NS
PPBS	293.48 ± 106.31	283.56 ± 82.73	t = 0.445, P = 0.657, NS

Study reveals that; mean FBS and PPBS were shown higher in the patients of DM with HTN as compare to DM without HTN but statistically not significant (P>0.05).

Table 3: Distribution of Uric acid level (SUA) between the individuals of group A and group B

Uric acid level SUA mg/dl	Group A		Group B		Total	
	No	%	No	%	No	%
2.5—3.5	2	2.7	9	12.0	11	7.3
3.6—4.5	9	12.0	9	12.0	18	12.0
4.6—5.5	12	16.0	13	17.3	25	16.7
5.6—6.5	10	13.3	20	26.7	30	20.0
6.6—7.5	15	20.0	16	21.3	31	20.7
7.6—8.5	20	26.6	6	8.0	26	17.3
8.6—9.5	5	6.7	2	2.7	7	4.7
>9.5	2	2.7	0	0.0	2	1.3
Total	75	100.0	75	100.0	150	100.0
Mean ± SD	6.66 ± 1.72		5.62 ± 1.51		6.14 ± 1.61	
P-value	t = 3.915 P = 0.000, HS					

Study reveals that; the mean of SUA in DM with HTN was 6.66 ± 1.72 mg/dl and the mean of SUA in DM without HTN was 5.62 ± 1.51 mg/dl, shows statistically highly significant difference of mean uric acid level (SUA) between the individuals of DM with HTN and DM without HTN (P<0.001). The SUA level was seen significantly higher in the individuals of DM with HTN as compare to patients of DM without HTN.

Table 4: Distribution of SUA levels in Group A and Group B females

SUA levels	Group A		Group B	
	Number	Percentage	Number	Percentage
< 2.5	0	0.0	0	0.0
2.5—6.0	16	43.2	26	60.46
> 6	21	56.8	17	39.5
Total	37		43	
X^2 test, P-value	X^2 = 2.963,		P = 0.227,	NS

Study revealed that; In group A, among females 0 (0%) had low,16 (43.2%) had normal and 21 (56.8%) high uric acid levels and in group B, 0 (0%) had low, 26 (60.46%) had normal and 17 (39.5%) high uric acid levels. The females with DM with HTN patients had comparatively higher SUA level than females with DM without HTN, which was statistically insignificant (P>0.05).

Table 5: Distribution of SUA levels in group A and group B males

SUA levels	DM with HTN		DM without HTN	
	Number	Percentage	Number	Percentage
< 3.5	0	0.0	1	3.1
3.5—7.0	16	42.1	26	81.3
> 7	22	57.9	5	15.6
Total	38	100.0	32	100.0
X^2 test, P-value	X^2 = 13.67,		P = 0.002, HS	

Study reveals that; among males 0 (0%) had low, 16 (42.1%) had normal and 22 (57.9%) high uric acid levels in group A and in group B 1 (3.1%) had low, 26 (81.3%) had normal and 5 (15.6%) high uric acid levels. The males with DM with HTN had higher level of SUA as compare to males with DM without HTN, which was statistically significant (P<0.01).

Table 6: Comparison of HbA1c between the individuals of group A and group B

HbA1c	Group A		Group B		Total	
	No	%	No	%	No	%
6.5—7.5	14	18.7	21	28.0	35	23.3
7.6—8.5	6	8.0	19	25.4	25	16.7
8.6—9.5	16	21.3	9	12.0	25	16.7
9.6—10.5	12	16.0	10	13.3	22	14.6
10.6—11.5	8	10.7	7	9.3	15	10.0
11.6—12.5	10	13.3	3	4.0	13	8.7
≥ 12.6	9	12.0	6	8.0	15	10.0
Total	75	100.0	75	100.0	150	100.0
Mean ± SD	9.92 ± 2.16		9.04 ± 2.10		9.48 ± 2.13	
P-value	t = 2.521		P = 0.013,		S	

Study reveals that; the mean of HbA1c in DM with HTN was 9.92 ± 2.16 % and the mean of HbA1c in DM without HTN was 9.04 ± 2.10 %. There was statistically significant difference of mean HbA1c level between both the groups (P<0.05).

Table 7: Correlation between mean HbA1c and Uric acid level (SUA) in the individuals of Group A

HbA1c levels	Number of patients	Mean HbA1c	Mean SUA
6.5—7.5	14	7.01	6.21
7.6—8.5	6	7.83	6.35
8.6—9.5	16	9.02	6.65
9.6—10.5	12	10.0	6.82
10.6—11.5	8	11.2	6.9
11.6—12.5	10	11.95	7.04
≥ 12.6	9	13.46	7.17
Correlation coefficient and P-value	r = +0.313	P< 0.01 Highly significant positive correlation	

Study reveals that; in group A, 14 individuals had mean HbA1C of 7.01% with mean SUA level of 6.21 mg/dl, 6 individuals had mean HbA1C of 7.83% with mean SUA level of 6.35 mg/dl, 16 individuals had mean HbA1C of 9.01% with mean SUA level of 6.65 mg/dl, 12 individuals had mean HbA1C of 10.0% with mean SUA level of 6.9 mg/dl, 8 individuals had mean HbA1C of 11.2% with mean SUA level of 6.9 mg/dl, 8 individuals had mean HbA1C of 11.95% with mean SUA level of 7.04 mg/dl, 9 individuals had mean HbA1C of 13.46% with mean SUA level of 7.17 mg/dl. There was a highly significant positive and linear correlation between HbA1c with Uric acid level

(SUA) in patients of DM with HTN (P<0.01, r = +0.313).

Table 8: Correlation between mean HbA1c and Uric acid level (SUA) in the individuals of Group B

HbA1c levels	Number of patients	Mean HbA1c	Mean SUA
6.5—7.5	21	6.9	5.15
7.6—8.5	19	8.09	5.25
8.6—9.5	9	9.05	5.43
9.6—10.5	10	10.1	5.88
10.6—11.5	7	10.6	6.1
11.6—12.5	3	11.5	6.35
≥ 12.6	6	12.1	6.8
Correlation coefficient and P-value	**r = +0.291**	**P< 0.05**	**Significant positive correlation**

Study revealed that; in group B, 21 individuals had mean HbA1C of 6.9% with mean SUA level of 5.15 mg/dl, 19 individuals had mean HbA1C of 8.09% with mean SUA level of 5.25 mg/dl, 9 individuals had mean HbA1C of 9.05% with mean SUA level of 5.43 mg/dl, 10 individuals had mean HbA1C of 10.1% with mean SUA level of 5.88 mg/dl, 7 individuals had mean HbA1C of 10.6% with mean SUA level of 6.1 mg/dl, 3 individuals had mean HbA1C of 11.5% with mean SUA level of 6.35 mg/dl, 6 individuals had mean HbA1C of 12.1% with mean SUA level of 6.8 mg/dl. There was a significant positive and linear correlation between HbA1c with Uric acid level (SUA) in patients of DM with HTN (P<0.05, r = +0.291).

DISCUSSION

Population aging is an obvious problem in the society, which affects the public health. According to a survey, the prevalence of diabetes and prediabetes among people aged 40–49 is 11.1% and 40.3%, respectively, while the prevalence of diabetes and prediabetes among people aged 60–69 has increased to 23.9% and 47.6%, respectively, as it proves advanced age is the major risk factor for prediabetes and diabetes6. In the study of Tripathi et al., 50 diabetics with HTN had mean age of .5±1.51 years and 50 normotensive diabetics had 50.4±1.46 years.[7] This study included 150 patients which were grouped into group A which included 75 T2 DM hypertensives and group B which included 75 normotensive diabetics. In this study, the mean age of group A was 52.80±9.25 years and the mean age of group B was55.25±9.21 years.

Hypertension is significantly affected by the gendered factors. There are sex-specific consequences of elevated blood pressure between males and females. In Ji H et al., study females exhibited a much sharper incline in blood pressure from the third decade of life.[8] Ultimately, suggesting there is a fundamental difference for increased blood pressure between the sexes and promotes sex-convergence of hypertension prevalence later in life. In the EHIS (N = 316,333, Females: 51.3%) and CCHS (N = 109,659, Females: 53.7%), 7.3 and 8.4% reported having diabetes mellitus, respectively.[9] There are sex differences in prevalence, symptoms, comorbidities, outcomes, treatments, and prevention of individuals with DM, as per current literature. For example, males with diabetes have a higher risk for microvascular complications, such as retinopathy and nephropathy, whereas several studies report a higher relative risk for cardiovascular diseases in females with diabetes compared to their male counterparts.[10] In the study of Alqahtani, et al., females were more compared to males i.e., out of 1984 patients 1215 (61.2%) were females and 769 (38.6%) were males123. In our study, out of 150 individuals, 80 (53.3%) were females and 70 (46.7%) were males, which was similar to his study.

HTN and DM, known to co-exist, have similar etiology, disease mechanisms and are influenced by various lifestyle factors, BMI is one of them. Multiple studies have shown that the overweight status, an independent risk-factor for diabetes, hypertension and dyslipidemia.[11]

In our study majority of individuals i.e., 54 (36.0%) were overweight, followed by 41 (27.3%) were normal weight, 36 (24.0%) and 18 (12.0%) were obese and obesity class-I respectively. The mean BMI score in group A was 28.90 ± 4.92 and the mean BMI score in group B was 27.58 ± 4.32, with p value of 0.082 suggests there was no statistically difference of BMI between group A and group B.

Ketema and Kibret in their study concluded that PPBS had a positive association with HbA1C than FBS and PPBS is better predictor of glycemic control in the absence of HbA1c.[12] In our study, the mean fasting blood sugars (FBS) and the postprandial blood sugars (PPBS) of the group A was 192.62 ± 72.32 mg/dl and 293.48 ± 106.31 mg/dl, respectively and in group B was 180.80 ± 56.60 mg/dl and 283.56 ± 82.73 mg/dl, respectively. Both these values were higher compared to the study by Shirsath, et al., which had the mean FBS 186.10 ±77.53 mg/dl and the mean PPBS was 274.94 ± 108.66 mg/dl.[13]

Current literature suggests that hyperuricemia (HU) will play a role in the development and pathogenesis of a number of hemodynamic, metabolic and systemic pathological diseases, including diabetes mellitus (DM).14 Nakanishi et al., study found that there was close association of SUA level with an increased risk for HTN and Type 2 diabetes.[15]

In the present study, even though both group A and group B had higher SUA level, it was significantly (p=0.0001) higher among group A patients (6.66 ± 1.72) as compared with group B patients (5.62 ± 1.51). Singh, et al., study shown that normotensive patients mean serum uric acid levels (5.29 ± 0.114) were lower than the mean serum uric acid levels of hypertensive patients (5.53 ± 0.131).[16]

In our study, 56.8% (n=21) females had serum uric acid levels of >6 mg/dl, 43.2% (n=16) had normal serum uric acid levels (2.5 – 6) and 57.9% (n=22) males had serum uric acid levels of >7 mg/dl and 42.1% (n=16) had normal serum uric acid levels (3.5 – 7 mg/dl), in group A. Similar results were obtained from the study Shirsath, et al., which had 80.39% of females has serum uric acid level of ≥ 6.3, rest (19.61%) had levels of 2.1–6.3 mg/dl.[12]

This study reveals that, the mean of HbA1c in group A [DM with HTN] was 9.92 ± 2.16 and the mean of HbA1c in group B [DM without HTN] was 9.04 ± 2.10, which was statistically significant (p<0.05). Omar et al., in their concluded that the HbA1c levels were significantly higher among patients with diagnosed hypertension compared to those who were non-hypertensive.

Our Study revealed that; there was statistically highly significant positive correlation between HbA1c with Uric acid level (SUA) in patients of group A (p <0.01, r = +0313) compared to that of group B (p <0.05, r = +0.291).

Selvakumar et al., study found that HbA1C was statistically highly significant positive correlation between SUA level in group 3 [DM with HTN with CAD].[17] Shirsath et al., revealed that highly significant association between HbA1c and Uric acid levels (p<0.001). With increasing levels of uric acid observed in subjects with HbA1c levels of ≥ 6.5.[12]

CONCLUSION

T2 DM with hypertension are more prone to develop hyperuricemia than without hypertension. SUA is linearly and positively associated with increase in levels of HbA1C in both the groups, which not only strengthened the close relationship between fluctuation of blood glucose levels and the risk of hypertension, but also made us to pay attention to the traditional risk factors of hypertension. Hence it is sensible to monitor serum uric acid levels, HbA1C levels and blood pressure in Type 2 Diabetes mellitus with or without hypertension, to prevent morbidity and mortality due to diabetic complications. In such patients care should be taken while prescribing drugs, food and other factors which increase SUA levels.

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