IRAETC Journal of Nursing and Health Care
ISSN (e): 3005-3838
Volume: 1 (2023), Issue: 1 (Sep-Oct)
OPEN ACCESS
iraetcjournals.com

Prevalence and Correlation of Hyperuricemia in Diabetes Patients: A Study at a Tertiary Level Hospital in Bangladesh

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Original Research Article

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Citation:
Ahmed Masiha Jamil & Rahnuma Shirin (2023); Prevalence and Correlation of Hyperuricemia in Diabetes Patients: A Study at a Tertiary Level Hospital in Bangladesh. iraetc j. nur. health care; 1(1) 8-12.

Abstract:

Background: The prevalence of hyperuricemia (HU), which has been associated to the emergence of cardiovascular disease, high blood pressure, the metabolic syndrome, and diabetes mellitus (DM), is on the rise. Serum uric acid (SUA) elevations have been linked to an increased risk of hypertension and diabetes in many nations. However, this association has not been established in the Asia region. ***Objective:*** The aim of this study is interested in the frequency of HU and the connection between Hyperuricemia with diabetes patient. ***Methods:*** This cross-sectional study was conducted in the Department of Medicine Rajshahi medical college, Rajshahi. Three hundred-five patients with a recent diagnosis of diabetes were enrolled (212 men and 93 women). Following American Heart Association guidelines, all patients were classified as having normal or high blood pressure (140/90). ***Results:*** The average SUA level was 5.14± 0.073 mg/dl, with males having considerably greater levels than females (P<0.000). The patients' mean age, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were 46.76 ±0.61 years, 130.6±1.06 mmHg and 84.11±0.63 mmHg, respectively. The overall prevalence of HU and hypertension was 12.13% and 44.59%, respectively. There was an increase in the prevalence of hypertension across the SUA tertile. SBP and DBP significantly increased across the SUA tertile (P<0.014 and <0.001, respectively). ***Conclusion:*** In Asia, this is the first study to investigate at the relationship between SUA and hypertension in diabetic people. Therefore, in newly diagnosed hypertensive diabetic patients, it is recommended to test SUA routinely to prevent HU and its related consequences.

Key Words: hypertension, prevalence, serum uric acid, diabetes mellitus.

|| © IRAETC Publisher || **Publication History -** Received: 04.07.2023 || Accepted: 12.09.2023 || Published: 16.09.2023||

INTRODUCTION

The prevalence of diabetes mellitus (DM) and associated comorbid cardiovascular disease is increasing (CVD).[1] Diabetics may lose as much as ten years of life expectancy, and cardiovascular disease is the primary killer of this population.[2] Diabetes-related cardiovascular disease (CVD) is associated with several metabolic abnormalities, including dysglycemia, hypertension, dyslipidemia, obesity, and hyperuricemia.[3] Controlling blood glucose alone is insufficient to prevent CVD in those with DM. That's why we need a fresh and multifaceted approach to preventing cardiovascular disease in people with diabetes. Additional methods of reducing the risk of CVD in DM include regulating blood pressure, cholesterol, and fat and protein levels, as well as uric acid and uric acid levels.[4]

Uric acid is produced during purine metabolism (UA). Elevated levels of this protein are present in individuals with obesity, insulin resistance, metabolic syndrome, and diabetes mellitus..[5] An increased UA serum level is linked to an increased risk of cardiovascular disease, endothelial dysfunction, chronic kidney disease (CKD), incident hypertension, and prediabetes .[6] Recent years have seen a surge in interest in the correlation between SUA and hypertension rates. Several epidemiological studies have indicated a correlation between SUA and hypertension.[7] But whether SUA is a marker for hypertension or a risk factor for the development of hypertension is not well established. Some think both conditions stem from the same root cause, such as a high-sugar diet leading to hyperuricemia and hypertension. There are two stages in the progression of hypertension caused by SUA .[8] First, it raises renin secretion, reduces nitric oxide bioavailability and increases oxidative stress. This first step leads to renal vasoconstriction, a reversible uric acid (UA) dependent and salt-inducible hypertension. After some weeks of persistently elevated UA, architectural vascular damage occurs with afferent arteriolopathy and mild interstitial inflammation. At this second stage, hypertension becomes salt sensitive and does not respond to UA- lowering therapy. Recently a few studies with small numbers of subjects have reported that UA-lowering therapy can reduce blood pressure in hypertensive patients with hyperuricemia.[9] This suggests that SUA might be a risk factor for hypertension. So, if we can reduce the uric acid with drugs (xanthine acid oxidase inhibitors) or lifestyle modification, we can prevent the development of hypertension and, thus, CVD. A positive association has been found between SUA and hypertension in various countries.

Furthermore, the level of SUA varies among different ethnicities due to genetics, diet and lifestyle differences. Hence, we aimed to investigate the association of SUA with hypertension in newly diagnosed diabetic patients from the eastern part of Asia region and further know the prevalence of hyperuricemia and hypertension in these diabetic patients.

MATERIALS AND METHODS

This cross-sectional tertiary care centre-based study was conducted between June 2020 and July 2021. Three hundred five consecutive patients with newly onset diabetes (duration <1 year) were enrolled over a period of one year. Patients with a history of renal, cardiac, or hepatic diseases, pregnant women, drug addicts and patients on anti-hyperuricemia treatment were excluded from the study.

Data regarding age, sex, height, weight, BMI (body mass index), waist circumference (WC), BP (blood pressure), uric acid, lipid profile, glycosylated hemoglobin A1c (GlyHbA1c), glomerular filtration rate (GFR) were collected from patients on a predefined format. Weight was measured by a weighing machine with a precision of 0.1 kg. A stadiometer measured height with a precision of 0.1 cm. For height measurement, patients were asked to remove footwear and stand with their head kept in the Frankfort position. BMI was calculated by dividing the weight (in kg) by the square of height (in meters). BP was measured with the help of a digital BP machine. 7 mL venous blood was collected in the morning for FPG (fasting plasma glucose), GlyHbA1c, vitamin D, creatinine and lipid profile. Blood glucose was estimated by the glucose oxidase-peroxidase method. Vitamin D level was analyzed on Siemens ADVIA centaur, standardized against ID-LC/MS/MS, as per vitamin D standardization (Thyrocare). Creatinine was measured by the creatinine enzymatic method. The lipid profile was carried out by standard enzymatic procedure. Ultrasonography was done to rule out cirrhosis in suspected cases.

The present investigation defined elevated SBP (systolic blood pressure) as ≥140 mmHg and/or DBP (diastolic blood pressure) ≥90 mm Hg as per ADA criteria. All hypertensive patients were either on amlodipine or telmisartan as they did not influence the serum uric acid level.

Hyperuricemia was defined as SUA level >416.4 micromole/mL (>7 mg/dl) in men and >356.9 micromole/mL (>6 mg/dl) in women. All participants were divided into three tertiles based on SUA levels (T1: <4.52 mg/dl; T2: 4.52–5.64 mg/dl; T3: >5.64 mg/dl). The prevalence of hypertension was estimated in each tertile separately.

RESULTS

Utilize and research descriptive statistics for populations. Table 1 summarizes the baseline characteristics of newly diagnosed diabetes individuals. 305 (Male: 212, Female: 93). Patients with a mean age of 46.76±0.61 years were recruited in the study. There was no significant age difference between the male and female groups. The mean BMI of patients were 26.33±0.25, with a significant difference between gender groups (P<0.04). The mean HDL (high-density lipoprotein) level was 41.32±0.56 mg/dl of all patients, and the mean HDL level was significantly higher in females compared with males (P <0.000). Females had a lower mean level of SUA compared with males (P <0.000). Mean levels of A1c, vitamin D, TG (triglyceride), WC, SBP, DBP, GFR, total cholesterol (TC) and LDL (low-density lipoprotein) were similar in the two groups. The prevalence of hyperuricemia was 12.13%, 11.79% and 12.90% in all males and females, respectively.

Table 1: Baseline Characteristics of the Study Participants by Gender. P-values are obtained from Independent Sample t-test in Comparison between the Gender Groups

Characteristics	Total (n = 305)			Male (n = 212)			Female (n = 93)			P-value
	Mean±SEm	Min	Max	Mean±SEm	Min	Max	Mean±SEm	Min	Max	
AGE	46.76±0.61	21	76	46.72±0.76	21.00	76.00	46.86±1.01	29.00	70.00	0.914
BMI	26.33±0.25	16.3	50.6	25.99±0.27	16.30	42.70	27.10±0.53	16.30	50.60	0.041
A1c	9.85±0.15	4.8	17.8	10.02±0.18	4.80	17.80	9.46±0.27	5.30	15.60	0.091
VIT D	19.26±0.59	4.2	76.6	19.73±0.68	4.85	75.00	18.20±1.17	4.20	76.60	0.233
TG	197.85±6.55	51	800	205.71±8.29	51.00	800.00	179.95±10.05	57.00	671.00	0.070
HDL	41.32±0.56	15	71	39.87±0.63	15.00	71.00	44.62±1.06	28.00	69.00	0.000
WC	97.11±0.54	71.5	130	97.28±0.66	71.50	126.00	96.70±0.97	78.00	130.00	0.621

SBP	130.60±1.06	85	190	130.50±1.25	85.00	190.00	130.83±1.98	90.00	180.00	0.885
DBP	84.11±0.63	60	140	84.63±0.75	60.00	140.00	82.92±1.15	60.00	110.00	0.213
Uric Acid	5.14±0.073	2.1	8.5	5.39±0.09	2.10	8.50	4.58±0.12	2.35	8.12	0.000
GFR	109.11±0.81	60.5	143	108.86±1.03	60.50	143.00	109.70±1.24	91.00	297.00	0.602
TC	184.02±2.44	89	345	182.72±3.02	89.00	345.00	186.98±4.07	31.00	205.00	0.421
LDL	109.99±2.12	31	237	107.94±2.55	33.00	237.00	114.67±3.80	29.00	70.00	0.145
Hyperuricemia	37 (12.13%)	-	-	25 (11.79%)	-	-	12 (12.90%)	-	-	-

SUA Tertile and Prevalence of Hypertension

The prevalence of hypertension in each tertile is presented in Table 3. The prevalence of hypertension was 44.59%. 44.34% and 45.16% in all, males and females, respectively. Prevalence of hypertension was similar in males and females. However, it increased with increasing concentration of SUA but more in females than males (P <0.05 for trends).

Table 3: Prevalence of Hypertension. Blood Pressure (mmHg) was Categorized as Normal (SBP < 140; DBP < 90) and Hypertensive (SBP ≥ 140; DBP ≥ 90)

Prevalence	Ter1 (<4.52)	Ter2 (4.52–5.64)	Ter3 (>5.64)	Total
Male	21 (38.89%)	32 (43.24%)	41 (48.81%)	94 (44.34%)
Female	16 (33.33%)	16 (57.14%)	10 (58.82%)	42 (45.16%)
Sub-Total	37 (36.27%)	48 (47.06%)	51 (50.50%)	136 (44.59%)

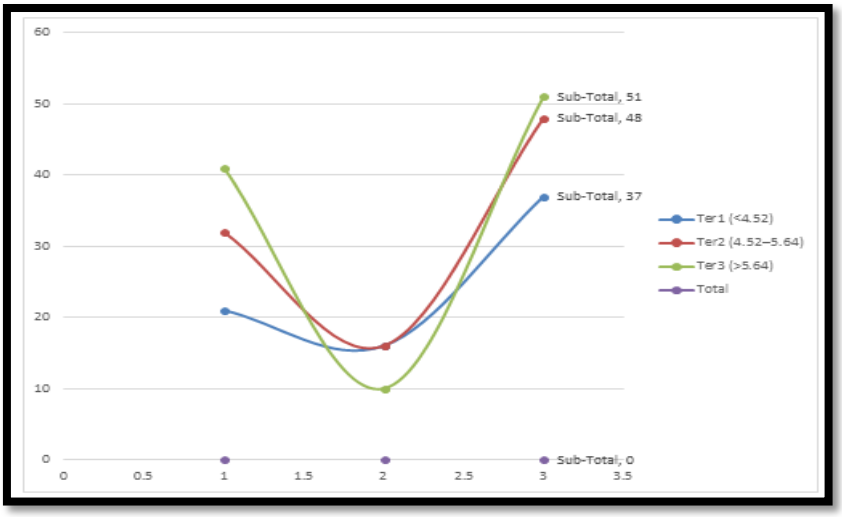

Figure 1: Blood Pressure (mmHg) was Categorized as Normal (SBP < 140; DBP < 90) and Hypertensive

Association of SUA Tertile with Blood Pressure

A significant positive correlation was found between SUA levels and SBP and DBP. Pearson's correlation coefficient test indicates that SUA level was significantly positively associated with SBP (r = 0.135, P <0.018) and DBP (r = 0.181, P<0.001) (Figure 1). In hypertensive patients, SUA was elevated compared with normotensive patients (Figure 2). The mean level of SUA in normotensive and hypertensive males was 5.29+0.114 and 5.53+0.131 with median (interquartile range) of 5.26 (2.06) and 5.49 (2.19) mg/dl, respectively. In females, mean levels of SUA in normotensive and hypertensive patients were 4.37+0.126 and 4.82+0.182 with median (interquartile range) of 4.26 (1.80) and 4.87 (1.88) mg/dl, respectively.

Table 4: Association of UA Quartiles with Hypertension. The Logistic Regressions were Applied to Evaluate the Association between SUA Quartiles and BP-Class

	OR (95% CI)			P-values
	Tertile1	Tertile2	Tertile3	

Model 1	1.000	1.092 (1.000–1.294)	1.153 (1.048–1.436)	<0.01
Model 2	1.000	0.980 (0.893–1.077)	1.040 (1.001–1.336)	<0.01
Model 3	1.000	1.114 (0.994–1.248)	1.287 (1.057–1.592)	<0.01

Notes: Model 1: Age and GFR were selected. Model 2: Age, GFR and Sex were adjusted. Model 3: Age, GFR, SEX and BMI.

Abbreviations: UA, uric acid; SAU, serum uric acid; BP, blood pressure; GFR, glomerular filtration rate; BMI, body mass index.

The associations of hypertension and SUA tertile for all diabetic patients are presented in Table 4 after applying logistic regression analysis. Hypertension was positively correlated with SUA tertile (P <0.01 for trends) in the present study. After adjusting age and GFR (model 1), the odds ratios (95% CI) were 1.092 (1.000–1.294) and 1.153 (1.048–1.436), respectively, for T2 and T3 compared with T1. In model 2, after adjustment for age, sex and GFR, the odds ratios (ORs) were 0.980 (0.893–1.077) and 1.040 (1.001–1.336) for T2 and T3, respectively, compared with T1. In model 3, after adjustment for age, sex, GFR and BMI, the ORs were 1.114 (0.994–1.248) and 1.287 (1.057–1.592), respectively, for T2 and T3 compared with T1. This shows that SUA tertile was independently associated with an increased prevalence of hypertension.

DISCUSSION

Hypertension is one of the main contributors to cardiovascular disease and early death. [10] All around the world, particularly in those with lower per capita incomes, the prevalence of hypertension has dramatically increased..[11] The differences in hypertension prevalence among regions may have multiple causes, including but not limited to dietary sodium intake, obesity, hyperuricemia, alcohol consumption, stress, physical inactivity, increased age, and an unhealthy diet. Despite its widespread presence, hypertension is poorly treated and controlled in the world's poorest nations. However, various trials show that if we can control blood pressure, we can reduce CVD. Meta-analysis shows that a 2 mmHg reduction in SBP can reduce stroke mortality by 10% and death from ischemic heart disease and other CVD by about 7%, and a further 2 mmHg reduction in DBP in the mean of population distribution can result in 6% decrease in the occurrence of CHD and 15% risk reduction of stroke and transient ischemic attack.[12] Primary hypertensive individuals, particularly malignant hypertensive patients, have been found to have hyperuricemia at high rates .[13] Recently a systematic review and meta-analysis by Agrawal *et al.* reported that treatment with a urate-lowering drug reduces SBP by 3.3 mmHg and DBP by 1.3 mmHg .[11] Therefore, reducing SUA can help lower blood pressure and, thus, CVD. In the present study, we tried to explore the prevalence of hypertension and hyperuricemia and the potential association between SUA and hypertension. This is the first study from eastern India that evaluated the relationship between SUA and hypertension in new-onset DM.

In the present study, the prevalence of hypertension was 44.59%, 44.34% and 45.16% in all males and females, respectively. Similar trends in the prevalence of hypertension were seen in previous studies also. Prevalence of hyperuricemia was 12.13%, 11.79% and 12.90% in all males and females. Similar results were found in other studies .[11] SUA was lower in females compared with males. The reason for low SUA in females is high estrogen levels. Estrogen is known to have uricosuric properties. Other reasons for high SUA in males are different eating habits, exercise and commuting methods.[14]

We also observed a relatively stronger relationship between SUA level and hypertension in females as compared to male diabetic patients. Other studies have also found the same. Gender-related differences were also reported in the association of SUA and MACE (major adverse cardiovascular event), arterial stiffness, metabolic syndrome, CAVI (Cardio-ankle vascular index) and cardiac diastolic dysfunction.[15] Although the reason for these gender differences is still unclear, sex hormones may have a role. Further studies are required to investigate the exact role of sex hormones in the development of hypertension and other related disorders in hyperuricemia patients.

Though vitamin D deficiency is associated with hyperuricemia in some reports, the causal association has always been a point of an enigma. In the present investigation, no significant association was found between uric acid and vitamin D levels. Such observations are also reported. Alcohol is known to increase serum uric acid levels in the blood. In the present study, patients were non-alcoholic except for very few patients who did not have alcohol consumption in the last seven days while collecting the samples. Since the effect of alcohol vanishes after 3 days, thus it has not influenced the statistical analysis.

There are three major caveats to this study. First, it is impossible to determine cause and effect due to its cross-sectional design. Second, there is a chance of bias due to the small size of the sample and the fact that it came from a single location. Third, as the SUA level is also reliant on a diet, we were unable to assess the patients' dietary habits.[16]

Earlier and more aggressive treatment of hyperuricemia will help prevent the problem, as the current study shows that hypertension is substantially and independently related to serum uric acid level.[17]

CONCLUSION

According to the current study's findings, SUA and hypertension are significantly positively correlated. In new-onset DM, hypertension and hyperuricemia are common.Multiple logistic regression analysis proves an independent relationship between SUA and hypertension. Therefore, routine measurement and treatment of SUA and blood pressure in diabetic patients is recommended to prevent the development of related complications.

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