DOI: https://doi.org/10.53350/pjmhs2023177192

ORIGINAL ARTICLE

Hyperuricemia in Patients with Type 2 Diabetes at Tertiary Care Hospital

HUMAIRA SAMI ULLAH
Department of Medicine, Unit II, Bolan Medical Complex Hospital, Quetta
Correspondence to: Humaira Sami Ullah, Email: drh.samiullah@gmail.com

ABSTRACT

Background: Hyperuricemia (HU) in Type 2 Diabetes Mellitus (T2DM), not only increases patient morbidity, but also lowers the quality of life, impairs functional ability, and increases mortality worldwide.

Objective: The aim of this study was to find out the frequency of Hyperuricemia in patients with Type 2 Diabetes Mellitus at tertiary care hospital.

Material and method: The current retrospective study was carried out at the Department of Medicine (Unit II), Bolan Medical Complex Hospital, Quetta, from 1st February 2022 to 30th January 2023. A total of 220 individuals of both genders and different age groups with type 2 diabetes mellitus were included. Data was collected using a non-probability consecutive sampling approach. Medical records were evaluated for the study without any direct patient interaction. For analysis, all of the data was collected and put into SPSS version 23.

Results: The medical record of 220 individuals with type 2 diabetes mellitus were examined in the present study. The mean age of the study participants was 56.6+11.8 years. Out of which female were 130 (59%) and male were 90 (41%). The individuals in the age group of 55 years or above were 129 (58.6%). The majority of patients had poor diabetes control 168 (76.3%). Ischemic heart disease was found in 31 (14%) individuals, nephropathy was recorded in 25 (11.3%) and hyperuricemia was found in 20 (9%) of the total individuals with type 2 diabetes mellitus. Hyperuricemia was found to have a significant statistical association with diabetes duration and nephropathy, when the data was stratified by gender, age, diabetes control, or ischemic heart disease. In particular, those with diabetes for six years or longer had a greater prevalence of hyperuricemia (n=18 or 15.2%) than people with diabetes for five years or less (n=4 or 4%). Similarly, there was a substantial correlation between nephropathy and hyperuricemia (p value= 0.009).

Conclusion: The present study concluded that hyperuricemia was seen in 9% of the patients with type 2 diabetes mellitus. This highlights the needs for mandatory serum uric acid screenings for all patients with type 2 diabetes mellitus. It will not only ensure early treatment for hyperuricemia, but that will in long term ultimately lead to reduction in morbidity and improvement in quality of life.

Key words: Type 2 Diabetes Mellitus T2DM, Hyperuricemia HU.

INTRODUCTION

The International Diabetes Federation estimates that 537 million people worldwide suffer from diabetes mellitus (DM), a number that is predicted to increase to 783 million by 2045.[1] Over 90% of cases of diabetes mellitus globally are Type 2 Diabetes (T2D), making it the most common kind of the disease.[2] The prevalence of type 2 diabetes in Pakistan is around 13%, indicating a substantial national cost.[3] Hyperuricemia ranks as one of the highest risk factors for developing diabetes mellitus in the normal poulation.[4] Type II diabetes is associated with hyperuricemia. Measuring serum uric acid is not a routine general practice unless vague and chronic musculoskeletal pains are complained or evident gout flare presents. Hence, HU may go undiagnosed.[5]

In the human body, uric acid is the ultimate product of purine metabolism. Intake of foods such as those with the umami flavor (rich in purines) and high fructose corn syrup have increased dramatically. Unlike other sugars, fructose can cause mitochondrial oxidative stress and inhibits AMPK, and the subsequent intracellular ATP depletion and nucleotide turnover lead to a significant increase in serum uric acid. Increased Uric Acid in Diabetes causes inflammation, by expression of interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-α, and C-Reactive Protein (CRP). Uric Acid mediated oxidative stress-induced lipid peroxidation, DNA damage, and activation of inflammatory factors finally lead to cellular damage. Oxidative stress also can affect the expression of insulin gene, causing a decrease in insulin secretion.[6] Diabetic nephropathy is one of the many adverse effects associated with hyperuricemia. DM and hyperuricemia share some similar mechanism for renal injury. On the other hand, hyperuricemia may lead to acute UA nephropathy, chronic urate nephropathy, gout related renal injury and NSAID related nephropathy.[7] Data from 2005–2006 showed that 47.1 million people in the US had hyperuricemia, which translates to a 20.1% overall prevalence rate.[8] Studies show that prevalence rates range from 11.3 to 47% in the United States, 11.9 to 25% in Europe, and 13.1 to 13.3% in China.[9] Several meta-analyses and systematic reviews have shown a robust correlation between hyperuricemia and type 2 diabetes in various groups. Interestingly, a recent worldwide meta-analysis revealed that, depending on the population under study, the overall incidence of diabetes among people with hyperuricemia varied from 16-19%.[10]

Few researchers has examined the incidence of hyperuricemia among diabetic individuals in tertiary care hospitals so far, despite Pakistan's high burden of type 2 diabetes and rising rates of metabolic syndrome associated hyperuricemia. Therefore the current study was conducted to find out the frequency of Hyperuricemia in patients with type 2 diabetes at tertiary care hospital.

Received on 11-04-2023
Accepted on 22-06-2023

MATERIAL AND METHOD

The current retrospective study was carried out at the department of Medicine, Unit II, Bolan Medical Complex Hospital, Quetta, from February 2022 to January 2023, after taking permissions. A total of 220 individuals of both genders and different age groups, with type 2 diabetes mellitus, were included. Patients with cancer or undergoing chemotherapy, those with end-stage renal disease, those with chronic liver disease, pregnant women, and those using medications that cause hyperuricemia, such as thiazide diuretics and anti-tuberculous treatment, were excluded from the study. T2DM was defined as HbA1c level of 6.5% or higher, a fasting plasma glucose level of 126 mg/dL or higher. Hyperuricemia was defined as serum uric acid >7.0 mg/dl in males and >6.0 mg/dl in females. Data was collected using a non-probability consecutive sampling approach. Medical records were evaluated for the study without any direct patient interaction. The criteria, which included uric acid, HbA1c, and blood sugar levels, were taken from medical records & from patient's most recent visit. A structured data collection sheet created especially to record important clinical and demographic information was used to collect data for the study. The data was collected by qualified medical specialists, who also made sure that it was accurate and consistent. They collected data by reviewing and evaluating medical records, paying particular attention to factors including age, gender, duration of diabetes, HbA1c levels, diabetes management, ischemic heart disease,

nephropathy status, as well as serum uric acid levels. For analysis, all of the data was collected and put into SPSS version 23. For numerical data, mean and standard deviation were computed, while for qualitative variables, percentage and frequency were generated. Stratification was used to control confounders and effect modifiers. After stratification, the Chi-Square and Fischer's exact tests were used, with a p-value of less than 0.05 were considered significant.

RESULTS

The medical record of 220 individuals with type 2 diabetes mellitus were examined in this study. The mean age of the study participants was 56.6+11.8 years. Out of which female were 130(59%) and male were 90(41%). Individuals in the age group of 55 years or above were 129(58.6%). The participants having diabetes for 6 years, or more, were 118(53.6%). The majority of patients had poor diabetes control 168(76.3%). Ischemic heart disease was found in 31(14%) individuals. Nephropathy was recorded in 25(11.3%) and Hyperuricemia was found in 20(9%) of the total individuals, with type 2 diabetes mellitus, as presented in table 1.

Table 1. Demographic features of the study participants

Features	Frequency/percentage
Age in years	
54 or below	91(41.3%)
55 or above	129(58.6%)
Sex	
Male	90(41%)
Female	130(59%)
Duration of diabetes	
5 years or below	102(46.3%)
6 years or above	118 (53.6%)
Control of diabetes	
Good / Controlled	52(23.6%)
Poor / Uncontrolled	168(76.3%).
Hyperuricemia	
Present	20(9%)
Absent	200(90%)
Ischemic Heart Disease	
Present	31(14%)
Absent	189(85%)
Nephropathy	
Present	25(11.3%)
Absent	195(88.6%)

Table 2. Stratification of data with respect to Hyperuricemia

Features	Hyperuricemia		Value of P
	Absent N= 200	Present N= 20	
Age in years			
54 or below	81(89%)	9(11%)	0.591
55 or above	119(92.2%)	10(7.7%)	
Sex			
Male	82(91%)	8(9%)	0.697
Female	119(91.5%)	11(8.4%)	
Duration of diabetes			0.038
5 years or below	98(96.0%)	4(4%)	
6 years or above	100(84.7%)	18(15.2%)	
Control of diabetes			0.764
Good / Controlled	48(92.3%)	4(7.6%)	
Poor / Uncontrolled	153(91%)	15(8.9%)	
Ischemic Heart Disease			
Present	20(64.5%)	11(35.4%)	1.43
Absent	178(94.1%)	11(5.8%)	
Nephropathy			
Present	20(80%)	5(20%)	0.009
Absent	180	15(7.6%)	

Hyperuricemia was found to have a significant statistical association with diabetes duration (p value 0.038) and nephropathy (p-value 0.009) when data was stratified by gender (p-value 0.698), age (p-value 0.591), diabetes control (p-value 0.764), or ischemic heart disease (p-value 0.143). In particular, those with diabetes for six years or longer had a greater prevalence of hyperuricemia (18, or 15.2%) than people with diabetes for five years or less (n=4, or 4%). Similarly, there was a substantial correlation between nephropathy and hyperuricemia, with 5 (20%) of patients with nephropathy and only 15 (7.6%) of those without it, as presented in table 2.

DISCUSSION

Type 2 diabetes mellitus (T2DM) is a chronic condition marked by hyperglycemia, brought on by, insufficient insulin production or insulin resistance. It significantly increases morbidity worldwide, impairs functional ability, lowers life quality, and increases patient mortality.[11] According to the International Diabetic Federation, diabetes affects 537 million adults worldwide and will cause nearly 6.7 million deaths in 2021. This makes diabetes a serious health burden, particularly in low- and middle-income nations like Pakistan where access to healthcare is already limited.[12]

Hyperuricemia has been associated with a poor prognosis in diabetic patients, including a higher risk of death and the development of diabetic squeal such neuropathy, retinopathy, and nephropathy. Uric acid, a result of purine metabolism, functions as an antioxidant to prevent atherosclerosis at first, but it also works as a pro-oxidant in advanced atherosclerosis.[13] Hyperuricemia contributes to atherosclerosis, which in turn causes coronary artery disease and other vascular conditions. Uric acid has recently been connected to changes in sugar intake as well as the development of type 2 diabetes, hypertension, and chronic kidney disease.[14-15] Endothelial dysfunction, elevated renin-angiotensin-aldosterone system activity, inflammatory pathways, and pro-fibrotic cytokine activation are thought to represent the pathophysiology of hyperuricemia. These modulators aid in the development of T2DM's micro-vascular problems, which lead to nephropathy and renal impairment.

Studies from Pakistan have shown a significant variance in the frequency of hyperuricemia in people with type 2 diabetes.[14] The present study was conducted to find out the frequency of hyperuricemia in patients with type 2 diabetes mellitus at tertiary care hospital. The medical record of 220 individuals with type 2 diabetes mellitus were examined in the present study. Out of which female were 130(59%) and male were 90(41%). Our study results are comparable to the study conducted by Mundhe SA et al in which females were most prevalent than male.[16] DM has been shown to be adversely affected by hyperuricemia. In the present study majority of patients had poor diabetes control 168(76.3%). According to one research, there is a 28% increased risk of adverse cardiovascular events for every 0.1 mmol/L rise in blood uric acid from baseline.[17] Ischemic heart disease was found in 31(14%) individuals with type 2 diabetes mellitus in our study. Hyperuricemia was found in 20(9%) of the total individuals with type 2 diabetes mellitus in our study. According to Alemayehu et al., hyperuricemia was seen in 27.28% of T2DM patients on the African continent, with a larger frequency in Central Africa (33.72%) than in North Africa (24.72%). However, there were no differences observed when comparing patient genders.[18] According to several studies, the prevalence rates of hyperuricemia in people with type 2 diabetes vary by nation, ranging from as high as 32.6% in China[19] to 16.6 percent in Australia (16.6%).[20] According to Arersa et al., 22.9% of T2DM patients had hyperuricemia, which is more frequent in older people, men, drinkers, obese patients, and those with long-term diabetes.[21] Our study explored that hyperuricemia was found to have a significant statistical association with diabetes duration and nephropathy when data was stratified by gender, age, diabetes control, or ischemic heart disease. In particular, those with diabetes for six years or longer had a greater prevalence of hyperuricemia (n=18, or 15.2%), which was strategically significant (p-value 0.038), than people with diabetes for five years or less (n=4, or 4%). Similarly, there was a substantial correlation between nephropathy and hyperuricemia, with 5 (20%) of hyperuricemia patients having nephropathy (p-value 0.009) which was strategically significant, while hyperuricemia was not associated with nephropathy 15

(7.6%). These findings are similar to other studies where hyperuricemia is associated with a high risk of nephropathy in T2DM patients. Raja et al. reported hyperuricemia in 17.9% of women and 39.9% of men in Karachi.[22]

Variations in environmental, economic, genetic, and sociocultural factors, as well as differences in the cut-off values used to label hyperuricemia, participant heterogeneity, research methodology, and awareness of risk factors for both hyperuricemia and type 2 diabetes mellitus, may be the cause for these national and international disparities in the prevalence of hyperuricemia in T2DM. Many factors, such as demographic characteristics, research scheduling, and laboratory techniques, may be blamed for the variations in hyperuricemia prevalence among different Pakistani studies on type 2 diabetic mellitus (T2DM). Prevalence rates are greatly impacted by differences in regional lifestyle and dietary practices, as well as demographic variations such as sex and age distribution. Furthermore, the chronological context of each research is important; variations in diabetes care and lifestyle variables over time may produce different outcomes. Additionally, various testing methodologies alter blood uric acid readings, and different diagnostic criteria for hyperuricemia are used in laboratories. Additional factors that may affect results include sample size, selection criteria, and research design, including cross-sectional and longitudinal studies. Variations in reported prevalence are also influenced by sociocultural variables, such as public education and knowledge of diabetes and its consequences. When taken as a whole, these factors highlight how difficult it is to determine the incidence of hyperuricemia in T2DM across various Pakistani studies.

Limitations of the study: The current research has many limitations. It was restricted to a single institution since it was a retrospective research. Additionally, we did not look at the effects of alcohol use, smoking, obesity, or hypertension. As a consequence, the findings may not apply to the broader population. However, further prospective cohort or case-control studies should be planned based on the results of this investigation to further emphasize the significance of hyperuricemia in type 2 diabetes and its consequences. Patients with type 2 diabetes should undergo routine screening for hyperuricemia and get early treatment for it.

CONCLUSION

The present study concluded that hyperuricemia was seen in 9% of the patients of type 2 diabetes mellitus**.** Moreover, hyperuricemia was statistically associated with nephropathy and the duration of diabetes, but not with age, gender, diabetes management, or ischemic heart disease. Patients with type 2 diabetes should have regular screenings for hyperuricemia and receive early treatment for it.

REFERENCES

1. Magliano DJ, Boyko EJ, Atlas ID. What is diabetes? IDF DIABETES ATLAS [Internet] 10th edition: International Diabetes Federation; 2021.
2. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119
3. Ayub R, Mustafa A, Ahsan J, Qureshi MG, Ali S, Inamullah M, Afaq F. To Assess the Frequency and Risk Factors of Type 2 Diabetes Mellitus in Adult Population of District Peshawar Pakistan. Pakistan Journal of Medical Research. 2022;61(4):145-9.
4. Fennoun H, Haraj NE, El Aziz S, Bensbaa S, Chadli A. Risk factors associated with hyperuricemia in patients with diabetes type 2: about 190 cases. Diabetes Research: Open Access. 2020;2020(1):12.
5. Raja S, Kumar A, Aahooja RD, Thakuria U, Ochani S, Shaukat F. Frequency of hyperuricemia and its risk factors in the adult population. Cureus. 2019;11(3)
6. Xiong Q, Liu J, Xu Y. Effects of Uric Acid on Diabetes Mellitus and its chronic complications. Int J Endocrinol. 2019; 10 (13). doi:10.1155/2019/9691345
7. Li C, Lee C, Hsieh Y, Chen C, Wu M, Tsai S. Li et al. Hyperuricemia and diabetes mellitus when occurred together have higher risks than alone on all-cause mortality and end-stage renal disease in patients with chronic kidney disease. BMC Nephrology (2022) 23:157. https://doi.org/10.1186/s12882-022-02755-1
8. Chen-Xu M, Yokose C, Rai SK, Pillinger MH, Choi HK. Contemporary prevalence of gout and hyperuricemia in the United States and decadal trends: the National Health and Nutrition Examination Survey, 2007–2016. Arthritis Rheumatol. 2019;71(6):991-9
9. Nutmakul T. A review on benefits of quercetin in hyperuricemia and gouty arthritis. Saudi Pharm J. 2022;30(7):918-26
10. Zhao R, Wang Y, Fu T, Zhou W, Ge X, Sha X, et al. Gout and risk of diabetes mellitus: meta-analysis of observational studies. Psychol Health Med. 2020;25(8):917-30
11. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33 Suppl 1(Suppl 1):S62-9. https://doi.org/10.2337/dc10- s062
12. Ramtahal R, Khan C, Maharaj-Khan K, Nallamothu S, Hinds A, Dhanoo A, et al. Prevalence of self-reported sleep duration and sleep habits in type 2 diabetes patients in South Trinidad. J Epidemiol Glob Health. 2015;5(4 Suppl 1):S35-43. https://doi.org/10.1016/j.jegh.2015.05.003
13. Patterson CC, Harjutsalo V, Rosenbauer J, Neu A, Cinek O, Skrivarhaug T, et al. Trends and cyclical variation in the incidence of childhood type 1 diabetes in 26 European centres in the 25 year period 1989-2013: a multicentre prospective registration study. Diabetologia. 2019;62(3):408-417. https://doi.org/10.1007/s00125- 018-4763-3
14. Shah N, Jamal S, Marwat MA. Association of hyperuricemia with diabetic nephropathy intype 2 diabetes mellitus. KJMS. 2014 Jul;7(2):267.
15. Li L, Song Q, Yang X. Lack of Associations between Elevated Serum Uric Acid and Components of Metabolic Syndrome Such as Hypertension, Dyslipidemia, and T2DM in Overweight and Obese Chinese Adults. J Diabetes Res. 2019;2019:3175418. https://doi.org/10.1155/2019/3175418
16. Mundhe SA, Mhasde DR. The study of prevalence of hyperuricemia and metabolic syndrome in type 2 diabetes mellitus. Int J Adv Med. 2016 May;3(2):241-9.
17. Xu Y, Zhu J, Gao L, et al. Hyperuricemia as an independent predictor of vascular complications and mortality in type 2 diabetes patients: a meta-analysis. PLoS One. 2013;8:e78206. [DOI] [PMC free article] [PubMed] [Google Scholar
18. Alemayehu E, Fiseha T, Bambo GM, Sahile Kebede S, Bisetegn H, Tilahun M, et al. Prevalence of hyperuricemia among type 2 diabetes mellitus patients in Africa: a systematic review and meta-analysis. BMC Endocr Disord. 2023;23(1):153. https://doi.org/10.1186/s12902-023-01408-0
19. Wang J, Chen RP, Lei L, Song QQ, Zhang RY, Li YB, et al. Prevalence and determinants of hyperuricemia in type 2 diabetes mellitus patients with central obesity in Guangdong Province in China. Asia Pac J Clin Nutr. 2013;22(4):590-8.
20. Ting K, Gill TK, Keen H, Tucker GR, Hill CL. Prevalence and associations of gout and hyperuricaemia: results from an Australian population-based study. Intern Med J. 2016;46(5):566-73
21. Arersa KK, Wondimnew T, Welde M, Husen TM. Prevalence and Determinants of Hyperuricemia in Type 2 Diabetes Mellitus Patients Attending Jimma Medical Center, Southwestern Ethiopia, 2019. Diabetes Metab Syndr Obes. 2020;13:2059-2067
22. Raja S, Kumar A, Aahooja RD, Thakuria U, Ochani S, Shaukat F. Frequency of Hyperuricemia and its Risk Factors in the Adult Population. Cureus. 2019;11(3):e4198. doi: 10.7759/cureus.4198.

This article may be cited as: Ullah HS; Hyperuricemia in Patients with Type 2 Diabetes at Tertiary Care Hospital. Pak J Med Health Sci 2023; 17(7):192-194.