

Serum uric acid level among type-2 diabetes subjects attending in a tertiary hospital of Bangladesh

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World Journal of Biology Pharmacy and Health Sciences, 2022, 12(01), 081–085

Publication history: Received on 02 September 2022; revised on 04 October 2022; accepted on 07 October 2022

Article DOI: <https://doi.org/10.30574/wjbphs.2022.12.1.0150>

Abstract

Introduction: Type 2 Diabetes mellitus (T2DM) is a heterogeneous disease which is characterized by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production. Serum uric acid, an end product of purine metabolism, has been shown to be associated with an increased risk of insulin resistance and components of the metabolic syndrome in previous epidemiological studies. However, the putative association of serum uric acid levels with type 2 diabetes mellitus is not clear. Therefore, the present study has been undertaken to determine the levels of explore the association of serum uric acid among male and female type 2 diabetic subjects.

Materials and Method: Under an observational analytical design a total of 104 T2DM (M/F, 40/64; age in years, 45±9; M±SD) were recruited. Among laboratory investigations, serum glucose was measured by glucose-oxidase method, lipid profile and serum uric acid by enzymatic colorimetric method.

Results: In male T2DM subjects, mean±SD fasting serum glucose (mmol/l) and 2hr after breakfast serum glucose were 7.99±1.45 and 10.93±2.24 respectively. In female T2DM subjects, mean±SD fasting serum glucose (mmol/l) and 2hr after breakfast serum glucose were 5.84±1.46 and 9.65±4.16 respectively. The 2hr after breakfast serum glucose was significantly higher in male T2DM subjects compared to female counterparts (p=0.026). In male T2DM subjects, mean±SD total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c) and very low-density lipoprotein cholesterol (VLDL-c) levels were 178.57±48.96, 144.30±72.20, 36.71±8.30, 137.80±34.14 and 28.86±14.44 respectively. In female T2DM subjects, these values were 186.21±47.946, 207.81±158.12, 39.43±13.12, 108.31±37.11 and 41.56±31.62 respectively. Among these lipidemic variables serum LDL-c was significantly higher in male T2DM subjects compared to female counterparts (p=0.050). Serum uric acid levels was significantly higher in male T2DM subjects compared to female counterparts (4.38±1.96 vs. 5.73±1.34, p=0.013).

Conclusion: From the above result it can be concluded that elevated level of serum uric acid is common in female T2DM subjects compared to male counterparts. Further studies with large sample size are warranted to explore the causal effects of this elevation. Therefore, uric acid serves as a potential biomarker of the glucose metabolism.

Keywords: Diabetes Mellitus; Glucose; Hyperuricemia; Nephropathy

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1. Introduction

Diabetes mellitus is a group of metabolic disease characterized by high blood glucose levels that results from defects in insulin secretion or action or both. It is a leading cause of morbidity and mortality. Prevention of diabetics and its associated burden, primarily cardiovascular morbidity and mortality, has become a health issue worldwide¹. Recent estimate indicates there were 171 million people in the world with diabetes in the year 2000 and this is projected to increase to 366 million in the developing countries, where it generally occurs in individuals aged 65 and above and six people die every minute from the disease worldwide, a figure that will soon make T2DM one of the world's most prevalent causes of preventable mortality². This devastating disease can affect nearly every organ system in the body. It can cause blindness lead to end stage renal disease, lower extremity amputations and neuropathy. Diabetic macro and micro vascular complications are resulting in increased disability and enormous health care costs³. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidney, nerves, heart and blood vessels⁴. Diabetes is the single most important metabolic disease, widely recognized as one of the leading causes of death and disability worldwide⁵. The number of people with type 2 diabetes is increasing rapidly in both developed and developing countries around the world. The emerging pandemic is driven by the combined effects of population aging, rising levels of obesity and inactivity.

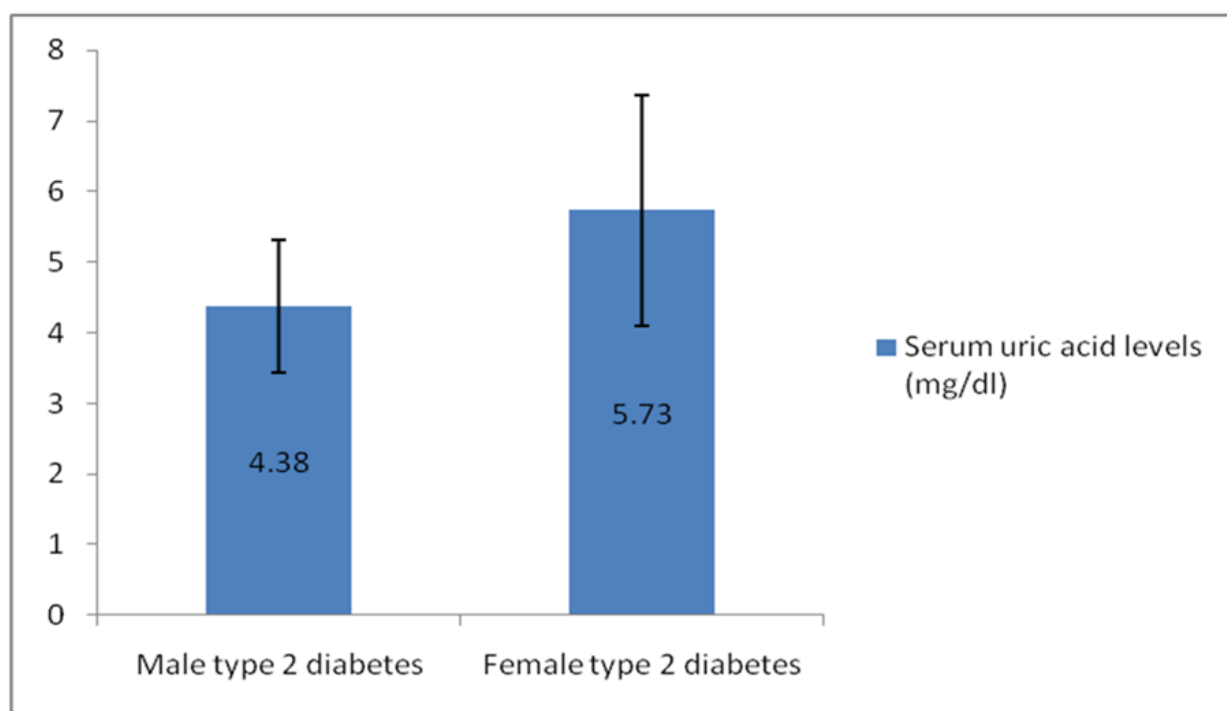


Figure 1 Serum uric acid levels of male and female T2 DM subject

There are several approximations about the global prevalence of diabetes. Diabetes mellitus has reached epidemic proportions worldwide, placing a substantial burden on health care services. However, recent estimates suggest that the prevalence of diabetes is rising globally, particularly in developing countries². Some population based studies concluded in Bangladesh at different time points have revealed an interesting trend of diabetes prevalence. In 2000, Bangladesh had 3.2 million with diabetes and was listed globally at 10th, which would occupy the 7th position with 11.1 million in 2030². The prevalence of diabetes in Bangladesh is 6.1% in 2010 and will be 7.4% in 2030⁶. Bangladesh is one of the 6 countries of the IDF SEA region. 382 million people have diabetes in the world and more than 72.1 million people in the SEA Region; by 2035 this will rise to 123 million. Classification of diabetes has been a difficult task. It used to be classified on the basis of age of onset presentation and need for insulin to treat. In early 50's it was classified as Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM).

Hyperuricemia is a risk factor for type 2 diabetes, but the causal association between them is controversial. A large epidemiological study⁷ of Japanese adult men showed that an elevation of serum uric acid levels increased the risk of type 2 diabetes. Although obesity has been recognized as a potential risk factor for type 2 diabetes, some studies on metabolic syndrome, diabetes, and hyperuricemia have documented high rates of type 2 diabetes in the absence of classical obesity among some populations. These results suggest that other independent pathogenic factors may exist

that could contribute to the occurrence of type 2 diabetes, with the development of type 2 diabetes⁸ demonstrated that serum uric acid is a strong and independent risk factor for diabetes in a 10-year follow-up study. Although decreased kidney function can be highly associated with hyperuricemia, based on some epidemiological studies, hyperuricemia is an independent risk factor for kidney dysfunction in patients with diabetes mellitus. The causal association between hyperuricemia and type 2 diabetes may be mediated by kidney dysfunction as well as insulin resistance. Although uric acid levels are substantially different between men and women most of the prior studies on this issue were conducted in male populations alone and, if including both men and women, did not conduct gender specific analyses⁷. Thus, it remains largely unknown whether there are gender differences regarding the relationship between uric acid levels and impaired glucose regulation.

2. Material and methods

It was an observational analytical study. The study was conducted in the outpatient Department of BIHS General Hospital, Dhaka, Bangladesh. The study was done during the period of August, 2018 to November, 2018. A total number of 104 T2DM subjects were recruited in this study. Among them 40 were male and 64 were female respectively. The inclusion criteria of this study were adult T2DM subjects with age ranging from 30-70 years and the exclusion criteria were patients suffering from any chronic systemic illness like hypertension, any renal diseases like stones, gestational DM, endocrine disorders, alcohol abuse. The general objective of the study was to determine the levels of serum uric acid among male and female type 2 diabetes subjects. Specific objectives are to determine the levels of uric acid among type 2 diabetes subjects, to determine the levels of uric acid among male type 2 diabetes subjects, to determine the levels of uric acid among female type 2 diabetes subjects. Statistical analysis was done using MS Excel for graph representation and SPSS 17.0 for the comparison between two groups. A P value <0.05 was considered statistical significant.

3. Results

3.1. Glycemic status of male and female T2DM subjects

Table 1 shows the glycemic status among male and female T2DM subjects. In male T2DM subjects, mean±SD fasting serum glucose (mmol/l) and 2hr after breakfast serum glucose were 7.99±1.45 and 10.93±2.24 respectively. In female T2DM subjects, mean±SD fasting serum glucose (mmol/l) and 2hr after breakfast serum glucose were 58.44±14.63 and 9.65±4.16 respectively. The 2hr after breakfast serum glucose was significantly higher in male T2DM subjects compared to female counterparts (p=0.026).

Table 1 Glycemic status of among male and female T2DM subjects

| Variables | Male T2DM subjects (n=40) | Female T2DM subjects(n=64) | t/p value |
|--|---------------------------|----------------------------|--------------|
| Age (years) | 49.90±15.50 | 58.44±14.63 | -0.413/0.74 |
| fasting serum glucose (mmol/l) | 7.99±1.45 | 9.65±4.16 | -0.453/0.163 |
| 2hr after breakfast serum glucose (mmol/l) | 10.93±2.24 | 14.69±5.66 | -2.375/0.026 |

Results were expressed as mean±SD, n=number of subjects.

3.2. Lipidemic status of male and female T2DM subject

Table 2 shows the lipidemic status of male and female T2DM subjects. In male T2DM subjects, mean±SD total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c) and very low density lipoprotein cholesterol (VLDL-c) levels were 07.57±48.96, 144.30±72.20, 36.71±8.30, 137.80±34.14 and 28.86±14.44 respectively. In female T2DM subjects, these values were 186.21±47.946, 207.81±158.12, 39.43±13.12, 108.31±37.11 and 41.56±31.62 respectively. Among these lipidemic variables serum LDL-c was significantly higher in male T2DM subjects compared to female counterparts (p=0.050).

Table 2 The lipidemic status of male and female T2DM subjects

| Variables | Male T2DM subjects(n=40) | Female T2DM subjects(n=64) | t/p value |
|---|--------------------------|----------------------------|--------------|
| Serum cholesterol (mg/dl) | 207.57±48.96 | 186.21±47.94 | 0.952/0.355 |
| Serum triglyceride (mg/dl) | 144.30±72.20 | 207.81±158.12 | -1.393/0.175 |
| Serum high density lipoprotein cholesterol (HDL-c) | 36.71±8.30 | 39.43±13.12 | -0.577/0.574 |
| Serum low density lipoprotein cholesterol (LDL-c) | 137.80±34.14 | 108.31±37.11 | 2.071/0.050 |
| Serum very low density lipoprotein cholesterol (VLDL-c) | 28.86±14.44 | 41.56±31.62 | -1.391/0.174 |

Results were expressed as mean±SD, n=number of subjects.

3.3. Serum uric acid levels of male and female T2DM subject

The bar diagram shows serum uric acid levels of male and female T2DM subject. In male T2DM subjects, mean±SD serum uric acid levels were 4.38±1.96. In female T2DM subjects, mean±SD serum uric acid levels were 5.73±1.34. Serum uric acid levels was significantly higher in female T2DM subjects compared to male counterparts (p=0.013).

4. Discussion

Several pathogenic processes are involved in the development of diabetes. This range from autoimmune destruction of the β -cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. The vast majority of cases of diabetes fall into two broad aetiopathogenic categories. In one category, type 1 diabetes, the cause is an absolute deficiency of insulin secretion. Individual at increased risk of developing this type of diabetes can often be identified by serological evidence of an autoimmune pathologic process occurring in the pancreatic islets and by genetic markers. The relative importance of defects in insulin secretion or in the peripheral action of the hormone in the occurrence of T2DM has been and will continue to be cause for discussion. Keeping in mind the intimate relationship between the secretion of insulin and the sensitivity of hormone action in the complicated control of glucose homeostasis, it is practically impossible to separate the contribution of each to the etiopathogenesis of T2DM. Serum uric acid is positively associated with serum glucose in healthy subjects. However; this association is not consistent between healthy and diabetic individuals, as a low serum level of uric acid is reported in the hyperglycemic state. Since most individuals experience a phase of impaired glucose tolerance before progression to diabetes, it is not clear whether raised serum uric acid predicts the risk of type 2 diabetes. Uric acid is the final oxidation product of purine metabolism in humans. There is evidence that hyperuricemia is associated with Uric acid is the final oxidation product of purine metabolism in the metabolic syndrome and incident type 2 diabetes. While some investigations found no association between uric acid levels and the risk of diabetes mellitus, in a recent meta-analysis a positive association was reported. A number of mechanisms have been suggested by which uric acid could affect changes in glucose metabolism. Elevated serum uric acid was found to be associated with oxidative stress and systemic inflammation both of which play crucial roles in the development of diabetes mellitus. Some studies reported that there is a positive association between elevated serum uric acid levels and diabetes⁹⁻¹¹, whereas some other study reported no positive association between serum uric acid and diabetes mellitus. Also, some studies reported that serum uric acid is inversely associated with diabetes mellitus¹². The exact reason for why previous studies found a positive relation between uric acid and diabetes is not clear. Most of these studies were limited by small sample sizes, including either men or women and not both, not having data on confounding factors. In our present study we found serum uric acid is significantly higher in male T2DM subjects compared to female counterparts (p=0.013). The elevation of serum uric acid, which is associated with impaired glucose tolerance and newly found type 2 diabetes, seemed to occur only in the presence of hyperinsulinemia which is apparently a cause as well as a consequence of insulin resistance. Similar results were reported¹³⁻¹⁴. Uric acid levels were significantly associated with different categories of impaired glucose regulation independent of known metabolic risk factors and lifestyle variables in men and women from the general population. The associations were more pronounced in women than in men. It could be shown that prediabetes subjects and persons with newly diagnosed diabetes had higher uric acid levels than normal glycemic subjects.

5. Conclusion

Serum uric acid level is higher among T2DM subject. From the above result it can be concluded that elevated level of serum uric acid is common in female T2DM subjects compared to male counterparts. Further studies with large sample size are warranted to explore the causal effects of this elevation. Therefore, uric acid serves as a potential biomarker of the glucose metabolism.

Limitations and recommendations

The study has several limitations -Sample size was small and other variables related to uric acid levels needs to be investigated to explore the causal association of elevated uric acid among male and female type 2 diabetes.

Compliance with ethical standards

Acknowledgments

The authors are grateful to Israt Ara Hossain, Senior Lecturer, Department of Biochemistry, Bangladesh University of Health Sciences (BUHS) for providing the laboratory facilities to carry out the part of the research work and Md. Ashiqur Rahman, Research Associate, CARS, University of Dhaka and Lab. Scientific Officer of Novus CRSL for helping in the preparation of this manuscript.

Disclosure of conflict of interest

The author hereby declares that there are no conflicts of interest concerning this paper.

Statement of informed consent

All participants gave signed informed consent before enrollment.

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