

Role of Hyperurecemia in Progress of Diabetic Nephropathy

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ABSTRACT

Background: Diabetes mellitus is very common in our community. Long standing and uncontrolled diabetes leads to various micro and macrovascular complications. Diabetic nephropathy is one of the common and deadly complication. It has been observed that in these patients along with elevated serum urea and creatinine, serum uric acid level was high.

Aim: To see the association of hyperuricemia and diabetic nephropathy.

Study design: It was a cross sectional observational study conducted at GTHS.

Method: Total 300 patients were enrolled in the study including both males and females of ages greater than or equal to 40 years. Only type 2 diabetic patients were included in our study. Patients of type 1 diabetes or drug induced diabetes (iatrogenic) or gestational diabetic or pre-diabetic patients were excluded. 150 patients with diabetes mellitus without any evidence of nephropathy (micro or macroalbuminuria) from outpatient department of GTHS were collected.

Results: Out of 150 patients in group 1, 72 (48%) were males and 78 (52%) were females. In male patients 55 (77.7%) were having serum uric acid within normal range. 16 patients (22%) were having impaired serum uric acid i.e. \geq or equal to 7 mg/dl. In female patients (78), 43 (55%) were having normal serum uric acid i.e. either \leq 6 mg/dl and 35 females (45%) were having high serum uric acid levels i.e. \geq or equal to 6 mg/dl. HbA1C level was mostly within desirable range in group 1 that is between 5 to 6 in 74% patients. Duration of diabetes was also less than 4 years in 67% patients. In group 2, 83 were males (55%) and 67 were (45%) females.

Conclusion: Diabetic nephropathy shows a positive relationship with increased serum uric acid levels. So, increased serum uric acid levels may be controlled by appropriate drugs and thus progress of diabetic nephropathy may be slowed

Keywords: Hyperurecemia, diabetic nephropathy, macroalbuminuria

INTRODUCTION

Renal impairment because of long standing uncontrolled diabetes mellitus is of the most common complication throughout the world^{1,2}. It is also recently observed that it is not only the duration and impaired glycemic control that contribute to diabetic nephropathy but increased serum uric acid may also play a key role in progress of nephropathy due to diabetes as it has been observed that it has an important role in development of hypertension, and diabetes and chronic kidney disease^{3,4,5}. It is already noted that it has an important contribution in nephropathy developing as a result of type 1 diabetes⁶. Serum uric acid may lead to development of diabetic nephropathy because it produces endothelial damage to the blood vessels^{7,8,9}. There are 2 possibilities that why people have increased serum uric acid levels, it can be increased production or decreased excretion. The later cause may be the reason of increased serum uric acid levels in diabetic nephropathy or it may result from increased tubular reabsorption¹⁰. This increased uric acid then further expedite the progress of diabetic nephropathy, and a vicious circle then starts leading to end stage renal disease. We as a doctor are doing several measures to control the progress of diabetic nephropathy, like tight glycemic control, control of blood pressure, angiotensin converting enzyme inhibitors^{11,12,13,14}. Now the purpose of this study is to see the association of increased serum uric acid levels with diabetic nephropathy, so that we may conduct studies to use uric acid lowering drugs in these patients that may stop or slow the progress of diabetic nephropathy.

MATERIAL AND METHODS

A cross sectional study was conducted at Govt Teaching Hospital Shahdara. It was an observation non-interventional study, in which equal number of diabetic patients with and

without diabetic nephropathy were taken, 150 from each group were enrolled in our study after taking informed written consent. They were properly interviewed and undergone various tests like BSF, BSR, HbA1C, urine C/E, if protein is positive in absence of infection or other causes of proteinuria like vigorous exercise or fasting and pregnancy then 24-hour urinary protein or spot urinary test will be performed to rule out or rule in diabetic nephropathy. Along with these tests blood urea and serum creatinine and serum uric acid levels will be carried out. Then percentages of patients with hyperuricemia in both groups will be noted and be compared to see any association between hyperuricemia and diabetic nephropathy. Along with calculating the %ages of hyperuricemia patients, %ages of pts with normal & impaired blood, glucose levels, percentages of patients with duration of diabetes with less than 5 years and more than 5-year duration, and patients with normal HbA1C (<6) and with impaired HbA1C (>6) were also noted and compared. Appropriate statistical tests were applied.

RESULTS

Two groups of diabetic patients were taken comprising of equal number of patients. 150 patients were in group 1 in which there were diabetic patients without nephropathy and in group 2 were 150 patients with diabetic nephropathy. In group of patients without nephropathy, 72 (48%) were males and 78 (52%) were females. In group 2, males were more predominant, i.e., 83 (55%) were males and 67 (45%) females. In patients without nephropathy i.e., group 1.

In group 1, 55 male patients (77.7%) were having serum uric acid within normal range and 16 patients (22%) were having impaired serum uric acid i.e. \geq or equal to 7 mg/dl. In 78 female patients, 43 (55%) were having normal serum uric acid i.e. either \leq 6 mg/dl and 35 females (45%) were having high serum uric acid levels i.e. \geq or equal to 6 mg/dl. HbA1C level was mostly within desirable range in group 1 that is between 5 to 6 in 74% patients. Duration of diabetes was also less than 4 years in 67% patients. In group 2, 83 were males (55%) and 67 were (45%) females. Mostly these patients have impaired HbA1C i.e. ≥ 8 or equal to 8. Duration was at least 7 years or greater in 63% patients. When their uric acid levels were checked 57% males and 69% males showed impaired uric

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acid levels. Most patients age were between 42±23 years. Out of these patients in group², 93, i.e., 62% were having frank proteinuria and 57(38%) were having microalbuminuria. This observation of hyperuricemia in most of patients of group 2 might indicate a positive relationship between diabetic nephropathy and hyperuricemia. Mostly these hyperuricemia patients in group 2 were also showing impaired blood glucose and HBA1C in majority of cases. Duration of diabetes was more than 7 years in 67% of patients in this group.

DISCUSSION

Our study showing positive relationship of hyperuricemia with diabetic nephropathy was in accordance to a study conducted by NS Neki, Himanshu Gupta et al¹⁵. In this study, they divided the patients in 3 groups. Group A was diabetic but without nephropathy, B group was the group in which there were patients with microalbuminuria and in group C were patients with frank proteinuria. The serum uric acid level in group A was mostly 3.12±2.10mg/dl, while in group C it was pretty high 6.80±3.45mg/dl. Another study was also in concordance with our study done by Bhagwat and Mane¹⁶.

In another study conducted by Fouad et al, showed increased level of serum uric acid in patients with diabetes and hypertension and one possible explanation of this increased uric acid was perhaps kidney disease associated with diabetes¹⁷. Several other studies have suggested a possible positive correlation between high serum uric acid and diabetic nephropathy^{18,19,20,21}. Naveen et al²² and Kundu et al²³ and Bushra Fiza et al²⁴ proves the same thing.

It is also interesting that there seems to be potential benefit of uric acid lowering drugs in patients of diabetic nephropathy as shown by an Egyptian study, but the patients in this study were not taking ACE inhibitors²⁵. The kidney disease of these patients got worst when uric acid lowering agents were withdrawn. Another study is being conducted in North America to see the usefulness of uric acid lowering drugs on progress of diabetic nephropathy²⁶. However, there are some flaws in our study which must be mentioned. Serum uric acid can also be elevated in obese patients, in diabetic patients with poor glycemic control and long duration of diabetes and in patients with hypertension and many other causes, so we sometimes may not decide that this increased uric acid is the cause of this diabetic nephropathy or in turn due to nephropathy, it remains unclear. Whatever the cause of increased serum uric acids there are evidences by the Egyptian study and study in North America that nephropathy is accelerated with increased serum uric acid levels and may be slowed down by decreasing levels of uric acid by uric acid lowering drugs.

CONCLUSION

So, it might be suggested that whatever the cause of hyperuricemia, it may play a role in progress of diabetic nephropathy because of its harmful effects on endothelium, and high levels of uric acid mostly in diabetic nephropathy group is an indirect evidence of this thing, and we need to conduct further studies on this issue on bigger scale. Further studies may be warranted to see the effect of uric acid lowering drugs on progress of diabetic nephropathy.

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