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Original Research Article

A Study on Serum Uric Acid and Proteinuria in Association with Diabetic Nephropathy among Type 2 Diabetic Patients in a Teritary Care Centre

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Abstract
Background: *Diabetes is the leading cause of end stage renal disease, adult-onset blindness, and non-traumatic lower limb amputations. Diabetic nephropathy (DN), is the leading cause of kidney diseases in patients starting renal replacement therapy and affects approximately 40% of type 1 and type 2 diabetic (T2D) patient). The pathogenesis of diabetic nephropathy include glycosylation of circulating and intrarenal proteins and abnormal intrarenalhemo dynamics. Recently various studies shows that level of serum uric acid was shown to be higher in diabetic patients with persistent macroalbumin*
Aims & Objectives: *To find out the association between serum uric acid and proteinuria level among type 2 diabetic patients attending a tertiary care centre.*
Subjects and Methods: A cross sectional study was carried out in the General medicine outpatient department of a tertiary care Centre. Diabetic nephropathy patients of both gender with no significant body weight changes for at least 3 months aged 30-60 years before the study are included in the study and Patients with Family history of gout, with known gout , on chemotherapy and known cancer patients are excluded.
Results: *Out of the 50 study participant's majority are females (60%). Mean ± SE of serum creatinine was 0.88 ± 0.038 mg/dL, mean ± SE of serum uric acid was 4± 0.12 mg/dl, and mean ± SE of proteinuria was 382 ± 24.7 mg/day (median = 300.5 mg/day.*
Conclusion: *serum uric acid plays a a major pathological role in the development of diabetic nephropathy in type 2 diabetic mellitus patients*
Keywords: *Serum uric acid, Diabetic nephropathy, Diabetic mellitus.*

Introduction

Diabetes is the leading cause of end stage renal disease, adult-onset blindness, and non-traumatic lower limb amputations[1]. Diabetic nephropathy (DN), is the leading cause of kidney diseases in patients starting renal replacement therapy and

affects approximately 40% of type 1 and type 2 diabetic (T2D) patient). The pathogenesis of diabetic nephropathy include glycosylation of circulating and intrarenal proteins and abnormal intrarenal hemodynamics. Hyperglycemia may cause increase mesangial cell glucose concentration and glycation of matrix proteins that lead to increased matrix production and mesangial cell apoptosis[2]. Cytokines activation, inflammation, and vascular growth factors may be responsible in the matrix accumulation in diabetic nephropathy[3]. Glomerular hypertension and hyperfiltration are also responsible for development and progression of in diabetic nephropathy, hence, blockade of the renin-angiotensin system is beneficial in the treatment of disease.It increases mortality mainly at the result of cardiovascular complications. Several factors which influence the development of diabetic nephropathy like the age, poor glycemic control, the most important role seems to be the inflammation and endothelial dysfunction.[4,5]. Recently various studies shows that level of serum uric acid was shown to be higher in diabetic patients with persistent macroalbuminuria[6]. Raised uric acid level is associated with endothelial dysfunction, insulin resistance, development of hypertension, and cardiovascular disease[7]. Elevated serum uric acid may be also associated with progression of non-diabetic renal disease[8]. Currently renin-angiotensin system blockade is the gold standard in diabetic nephropathy treatment that lead to slowing the renal impairment but not arrest or reverse of the disease. Thus we require adjunctive therapeutic strategies, especially in patients with complications of treatment or lack of appropriate response. Recently, some prospective randomized controlled trials suggested that lowering of uric acid with allopurinol could decrease the severity of proteinuria and probably slow the progression of renal failure in diabetic patients and also in the patients with hyperuricemia and non-diabetic chronic kidney disease Mechanism of beneficial effect of xanthine oxidase inhibitor may related to preventing uric acid-induced renal inflammation . Indeed, allopurinol decrease serum uric acid level and reduce oxidative stress, it is not exactly obvious the main beneficial mechanism of allopurinol in the diabetic nephropathy[9]. In conclusion, it seems that further studies are needed to clarify the effect of uric acid in initiation and progression of diabetic nephropathy and effect of uric acid lowering drugs on preventing or slowing of disease progression[10,11]. In view of the above statements we considered this study to find out if there is any association between serum uric acid level and proteinuria levels in diabetic patients.

Aims & Objectives

To find out the association between serum uric acid and proteinuria level among type 2 diabetic patients attending a tertiary care centre

Materials And Methods

Study design: Prospective Cross sectional Study

Study setting: General Medicine Department Sree Mookambika Institute of Medical Sciences Kulasekharam

Approximate total duration of the study: 6 Months (March 2016-August 2016)

Detailed description of the groups: Diabetic Nephropathy patients aged 30-60 years of both gender.

Total sample size of the study: 50 diabetic nephropathy patients

Scientific basis of sample size used in the study: As we took all the diabetic nephropathy cases who met the inclusion criteria in the 6 month period so there will be no sample size

Sampling technique used in the study: Convenient sampling

Inclusion criteria:

a) Diabetic nephropathy patients with no significant body weight changes for at least 3 months before the study.
b) Age group between 30-60 years, Patients willing to take part in the study

Exclusion criteria: Patients with Family history of gout, with known gout, on chemotherapy and known cancer patients**,**

Parameters to be studied: Serum Creatinine (mg/dl), Serum Uric acid(mg/dl) and serum Proteinuria (mg/dl)

Procedure in detail: After getting approval from Institutional Human Ethical Committee written informed consent was obtained from the patient before enrolling them into study. A detailed relevant history of patients were recorded including current medications, insulin doses, tobacco use, and family medical history were obtained. A thorough general physical examination with reference to pulse ,blood pressure, Temperature, respiratory rate were noted followed by Cardio vascular system, Central nervous system, Respiratory system, are examined.. Venous blood samples were obtained in fasting state for determinations of serum creatinine, uric acid, and hemoglobin A_{1c} (HbA_{1c}) (reference range 3.8-5.5%); 24-h urine proteinuria was also measured.

Data Analysis: The study Parameters entered in Microsoft Excel spread sheet and statistically analysed using program R, Version 3.00. Results were expressed as mean ± standard deviation (SD) and results which were having a $P < 0.05$ was considered as statistically significant

Results

Out of the 50 type 2 diabetic patients were participated in the study majority are females 60%. Majority of the participants belonging to lower socio economic status family (60%).65% of them had family history of diabetes mellitus.35% of the participants had consume tobacco and alcohol. Duration of type 2 diabetes mellitus among participants ranges from a minimum of 5 years to the maximum of 20 years with mean 4 ± 9SE . Mean ± SE of serum creatinine was 0.88 ± 0.038 mg/dL, mean ± SE of serum uric acid was 4± 0.12 mg/dl, and mean ± SE of proteinuria was 382 ± 24.7 mg/day (median = 300.5 mg/day). In this study, there was a significant positive association between body mass index and serum uric acid ($r = 0.428$, $P = 0.001$).

Discussion

Diabetes mellitus is a fastly growing disease which has come as gift to India with the adaptation to westernization, industrialization and competitive stressful life. When the statistics of the world are glanced this disease continues to be the fore runner of end-stage renal disease in India and most parts of the world. Once set in diabetic nephropathy is considered as a progressive disease which cannot be reversed. End-stage renal disease is one of the most draining stage which requires lifelong renal replacement which makes the diabetic a burden to the family and the society at large in terms of social life and financial drains. In the current study the mean serum creatinine level found to be 0.88 ± 0.038 mg/dL which is in accordance with Saeed et al[12] and Vinod et al in Manglore[13]. In the current study mean serum uric acid level found to be 4± 0.12 mg/dL which is similar to the findings done by saeed et al[12]. Various studies have shown that hyperuricemia may have a pathogenic role in the development and progression of chronic renal failure. In diabetic patients, serum uric acid early in the course of diabetes is significantly associated with later development of persistent macroalbuminuria[14,15]. Fukui *et al*[16] *also* showed a positive correlation of serum uric acid and urinary albumin excretion in persons with type 2 diabetes mellitus. They concluded that serum uric acid concentration is associated with microalbuminuria and subclinical atherosclerosis in men with type 2 diabetes mellitus. In this study, we found the significant positive association of serum uric acid with level of proteinuria, there is a well established association of hyperuricemia with obesity and various components of metabolic syndrome and chronic renal failure. There are documented studies which argue that hyperuricemia may have a pathogenic role in the development and progression of chronic renal failure, and may not be just due to decreased renal uric acid excretion. Similarly studies done Hovindet al[15] and Johnson et.al[17] also showed that elevation of serum uric acid early in the course of diabetes mellitus has a significant association with

development of macroalbuminuria in the later stages of the disease. These studies also concluded that renin–angiotensin system is the responsible system for renal damage in hyperuricemic conditions. Various studies also shown that hyperuricemia can cause various damages like the arteriolopathy of preglomerular vessels, impaired auto regulation, glomerular hypertension and endothelial dysfunction

Limitation: Minimal Sample size

Source of Funding; Self

Conclusion

Our study concluded that serum uric acid had a positive association with diabetic nephropathy. Taking this into account serum uric acid plays a a major pathological role in the development of diabetic nephropathy in type 2 diabetic mellitus patients

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