ASSOCIATION OF HYPERURICEMIA WITH DIABETIC NEPHROPATHY INTYPE 2 DIABETES MELLITUS

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ABSRACT

Objective: To determine the association of hyperuricemia with diabetic nephropathy in the patients of Type 2 diabetes mellitus.

Methodology: This descriptive and cross sectional study was performed in the Medical Unit of Hayatabad Medical Complex, Peshawar, Pakistan from April 2013 to December 2013. We included 163 diagnosed cases of type 2 diabetes mellitus in this study. The patients were collected from the hospital OPD and wards. Along with other routine investigations, blood urea, creatinie, fasting blood sugar, urine for albumen and serum uric acid levels were performed from the same laboratory on more than one occasion. Serum uric acid level of 7mg% in male and 6.5mg% or above in female was labeled as hyperuricemia. Albumen urea or createnine level of 1.3mg% or more was labeled as nephropathy in the patients of type 2 diabetes mellitus. Patients having reasons for hyperuricemia and albumen urea other than type 2 diabetes mellitus (see full text), were excluded from the study.

Results: One hundred and sixty three (163) diagnosed cases of type 2 diabetes mellitus were enrolled for the study. Forty six percent (n=75) were male and 54% (n=88) were females. Their age range was 34 to 90 years (mean 59.8 ±10.3). Fifty four percent (n=88) of our patients were hypertensive. The majority 78% (n=127) of the subjects were on oral hypoglycemic agent, 9% (n=15) were on insulin treatment and 13 % (n=21) were on a combination of oral hypoglycemic agents and insulin. A higher mean waist circumference and BMI was noted in females (94.6±8.5 cm and 28) as compared to males (91.4±9.6 cm and 26.5). Twenty-five percent (n=41) patients were having hyperuricemia. It tends to be a bit higher in the females 30.76% (n=25) than males 20% (n=16). There was no age difference between subjects with hyperuricaemia and normouricaemic subjects (60±10 vs 59.7±10.5). About nineteen percent (n=32) were having diabetic nephropathy with and without impaired renal functions. Overall hyperuricemia was more prevalent in patients with diabetic nephropathy 50% (n=16) than those without nephropathy 19% (n=25).

Conclusion: Overall hyperuricemia is common in type 2 diabetic patients and amongst these patients; it is comparatively more common in the patients of diabetic nephropathy. This factor is independent of gout and occasionally patients have been treated as gout with osteoarthritis of different joints which is quit common in these patients. Whether these patients need to be treated for hyperuricemia, is out of the scope of this study.

Key Words: Type 2 diabetes mellitus, diabetic nephropathy, hyperuricemia, albumenurea.

INTRODUCTION

Uric acid is end product of purine metabolism; it is filtered in glomeruli and excreted in urine. Hyperuricemia is defined by serum uric acid concentration greater than 7 mg/dl in man and 6 mg/dl in women.[1] Hyperuricemia due to genetic abnormality in the purine metabolism is a well known cause of gout. Hyperuricemia is present in normal population by about 14% in males and 1% in females as compared to its 32% prevelance in type 2 diabrtetic patients[2]. The frequency of hyperuricemia is more in the obese type 2 diabetic patients than those without obesity[3]. Similarly other literature has mentioned its association with metabolic syndrome or insulin resistance[4].

Apart from this, hyperuricemia is an associated factor with multiple other disorders. Uric acid is a common risk factor for, vascular diseases[5], hypertension[6], type 2 diabetes mellitus and diabetic nephropathy[7]. Hyperuricemia has an association with type 2 diabetes mellitus and hypertension independently of each other. It is more commonly associated with albumen urea than those without albumen urea in type 2 diabetic patients[7].

Though the cause and effect relationship of hyperuricemia and diabetic nephropathy is debatable, however some literature mentions the detrimental effects of high uric acid level on the kidney functions[8]. The main detrimental effect of high uric level as a part of the obesity and metabolic syndrome, is through its injurious effects on the endothelium and inducing chronic inflammation[9]. Some studies have shown slowing the progression of renal disease by treating the hyperuricemia with allopurinol[6].

The aims of this study were to find out the frequency of hyperuricemia in type 2 diabetes mellitus and compare it with that in the diabetic nephropathy in type 2 diabetics. Through these findings, this study will try to find out the association of hyperuricemia with diabetic nephropathy in the patients of type 2 diabetes mellitus.

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METHODOLOGY

This descriptive and cross sectional study was performed in the Medical unit of Hayatabad Medical Complex, Peshawar, Pakistan. One sixty-three type 2 diabetic patients were enrolled for the study. All the patients were collected from the hospital OPD and wards. Apart from thorough clinical examination, the patients were investigated for urine RE and macroalbumin urea, random blood sugar, CBC, S uric acid and renal functions including creatinine clearance (GFR). These investigations were performed from the hospital laboratory for more than one occasion. Hyperuricemia was defined as S uric acid level of 7mg% or above in males and 6.5mg% or above in females. Albumen urea or createnine level of 1.3mg% or more was labeled as nephropathy in the patients of type 2 diabetes mellitus. Those patients who were having protein urea due to causes other than diabetes mellitus, like urinary tract infection and glomerulonephritis as evidenced by the urine examination or past record, were excluded from the study. Similarly patients with diagnosed chronic kidney diseases due other causes as evidenced by the past investigations or small shrunken kidneys on ultrasound, were also excluded from the study. Patients with hyperuricemia due to gout or other unrelated illnesses like myeloprolirerative disorders as evidenced by the clinical status and investigations of the patients, were also excluded from the study.

RESULTS

One sixty three (163) diagnosed type 2 diabetic patients were enrolled for the study. Forty six percent (n=75) were male and 54% (n=88) were females. There was no major difference between the age range of male and female gender. The age range was 34 to 90 years with a mean of 59.8 ± 10.3. There was no significant difference of age in the hyperuricemic and normouricemic subjects (Table 1). Over all frequency of hypertension in our patients was 54% (n=88). The overall tendency of obesity was more in the females as compared to the males. The waist circumference and BMI was found to be 94.6±8.5 cm and 28) as compared to males (91.4±9.6 cm and 26.5). The values of different variables in normouricemic versus hyperuricemic patients are shown in Table 1. We also compared the average uric acid levels amongst hypertensive vs non hypertensive, diabetic nephropathy vs no diabetic nephrpathy, obese vs non obese and the effects of age in our study patients as shown in Table 2.

The overall prevelance of hyperurecemia was 25% (n=41) with a mean uric level of 7.8 ± 1.4 in our study patients. The gender was not significant as far as the hyperurecemia and normourecemia was concerned, though the mean uric acid level amongst the hyperurecemic patients, tends to be higher (8.23 ± 1.2mg%) in the males as compared to (7.43 ± 1.4mg%) the females. Similar effects were found with the age and weight of the patients as well (Table 2).

This study also showed that the prevalence of hyperuricemia is high in the patients of diabetic nephropathy as compared to those with no nephropathy. About nineteen percent (n=32) were having diabetic nephropathy with and without impaired renal functions. Overall hyperuricemia was 50% (n=16) in patients with

Table 1: Comparison of some clinical and biochemical parameters between normouricaemic and hyperuricaemic patients

Variable	Normouricaemic subjects	Hyperuricaemic subjects	P value
Age (years)	62.1(±10.5)	61.7(±10)	0.09
BMI(kg/m2)	28.2 (±5.6)	28.9 (±6.4)	0.3
Waist Circumference (cm)	92.8 (±12)	96.1(±14.5)	0.05
Duration of DM (years)	6.7(m=6) years	7.2(m=6.9) years	0.2
FBS (mg %)	167 (m=75)	170.5 (m=80.5)	0.6

Table 2: Showing the mean uric acid level in different groups of our study patients

Condition	Average uric acid level mg%	Hyperuricemia % age
Pt with hypertension (no D neph)	5.5 4±2.6	22
Pt with no hypertension (no D neph)	5.1 4±2.4	19
Pt with diabetic nephropathy	6.5 2±2.5	50
Pt with obesity (BMI-26 or above) (no D neph)	5.43 ±1.8	24
Pt with no obesity (BMI- <25) (no D neph)	5.13 ± 2.5	17
Age 34 to 49 years. (no D neph)	5.19 +2.34	17
Age 50 or above (no D neph)	5.41 ±2.4	21

D Neph……Diabetic nephropathy.

diabetic nephropathy than those without nephropathy 19% (n=25).

DISCUSSION

Apart from various well-known risk factors for cardiovascular disease, high uric acid level is increasingly recognized as a significant risk factor too. Apart from its association with cardiovascular diseases, we found the association of higher uric level with type 2 diabetes. This study reports the frequency of hyperuricemia in type 2 diabetics to be 25% verses 3-13% in the general population[10]. Madiannov etal mentioned a frequency of 30% in the type 2 diabetic patients[11]. A study in China reported the frequency of hyperuricemia in type 2 diabetic patients as 32.6%[12], while another Chinese study mentioned it as 15.55%[13]. All these studies show the frequency of hyperuricemia in type 2 diabetes higher than that in the general population.

This association was more with diabetic nephropathy as compared to those without diabetic nephropathy. Other literature also mentioned the association of hyperuricemia with albumenurea and diabetic nephropathy[14]. This study reports 50% prevalence of hyperuricemia in type 2 diabetic patients with nephropathy. An Iranian study also reports that 27.5% of the type 2 diabetic patients with nephropathy were in the quartile of uric acid > 5.3mg/dl as compared to 18.5% in the patients without nephropathy15 indicating the higher frequency of hyperuricemia in the patients with diabetic nephropathy as compared to the patients without diabetic nephropathy.

We also found the higher frequency of central obesity in the patients with hyperuricemia as compared to those without hyperuricemia (Table 1). Other literature also mentioned the association of central obesity with hyperuricemia[16]. Some literature points towards the facts that high uric acid level may be a new player in the development of diabetic nephropathy, so the significance of its treatment to reduce the progression to nephropathy[17]. This study also reveals the significance of high uric acid level in association with type 2 diabetes mellitus and even more so with diabetic nephropathy. So prospects regarding the slowing of nephropathy by treating hyperuricemia exist which needs further studies.

CONCLUSION

Hyperuricemia is a common association with type 2 diabetes mellitus. It has more strong association with diabetic nephropathy. Treating hyperuricemia may be important in preventing the diabetic nephropathy or slowing the progression in already established nephropathy. This needs further studies to know the role of treating hyperuricemia in preventing or slowing the progression of diabetic nephropathy.

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