ASSOCIATION OF SERUM URIC ACID WITH DIABETES MELLITUS IN DISTRICT NOWSHERA KPK

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ABSTRACT

Objectives: To compare the level of uric acid in diabetic and non-diabetic populations of District Nowshera

Methods: This Cross-sectional observational study was conducted in Department of Biochemistry Nowshera Medical College & Qazi Hussain Ahmed Medical Complex Nowshera from January-December 2018. Both male and female patients from 24-65 years were included in this study. Nearly one hundred samples were collected from selected patients for further investigation of serum Uric Acid and Blood glucose level.

Results: The number of cases having no diabetes were 77% out of which 59% of the patient had normal uric acid while 18% of the patient had abnormal uric acid. The number of cases having diabetes was 23% out of which 17% of the patients had normal uric acid while 6% of the patients had abnormal uric acid.

Conclusion: 6 percent Diabetics patients of Nowshera District had abnormal uric acid while 18 percent of Non-Diabetics patients had abnormal uric acid in our present study.

Key words: Hyperuricemia, gout, Hyperglycemia ,Hypoglycemia ,Diabetic ketoacidosis

INTRODUCTION

Uric acid ($C_5H_4N_4O_3$) is a heterocyclic, purine derivative bicyclic compound, consists of carbon, nitrogen, oxygen, and hydrogen. It is a diprotic acid ($pKa1=5.4$ and $pKa2=10.3$)[1]. It forms ions and salts like urates and acid urates like ammonium acid urate. It is a product of purine nucleotides metabolism. It high concentration causes gout and is associated with other medical conditions including diabetes and the formation of renal stones.

Uric acid So, in alkaline solution and high pH, it forms the dually charged full urate ion. in the presence of carbonic acid or biological pH, it forms the singly charged hydrogen or acid urate ion.due to its weak second ionization property, the full urate salts tend to hydrolyze back into hydrogen urate salts and free base at neutral pH.

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X-Ray studies in gouty crystals show that the keto-oxygen in the second position of the purine structure has an hydroxyl group and the two nitrogen atoms which share the ionic charge[2].

It was first isolated from renal stones in 1776. In 1882, Ivan Horbaczewski claimed to synthesized it from urea hydrogen peroxide, trichlorolactic acid, and its amide and glycine. However, Eduard Hoffmann contradicted Ivan methods that this preparation with glycine dose does not give a trace of uric acid. Rather, trichlorolacetamide forms some uric acid. Hence, Hoffmann appeared the first one to synthesize uric acid[3].

Diabetes mellitus, a multifactorial endocrine disorder is defined as high fasting blood glucose level caused by a relative or absolute deficiency in insulin. One of the leading cause of adult blindness, amputation, renal failure, nerve damage, heart attacks, and strokes.

Type 1 Diabetes Mellitus is is due to an absolute insulin deficiency caused by autoimmune destruction of β cells of the pancreas. In this, activated T-lymphocytes attack the islets of Langerhans, and as time passes, the β cells population vanishes. However, the patient becomes symptomatic abruptly when 80-90% of β cells depleted. At the point, the pancreas can not fulfill the insulin requirement, and exogenous insulin therapy is required to restore metabolic control of glucose regulation. β cells destruction requires both a stimulus from the environment (such as a viral infection) and a genetic determinant monozygotic (identical) twins, if one sibling develops Type 1 diabetes mellitus, the other twin has only 30 – 50% chance of developing the disease. However, in Type 2 disease, the genetic influence is stronger, and in virtually all monozygotic twinships, the

disease eventually develops in both individuals.

Type 2 diabetes develops gradually without prominent symptoms and is often detected by routine screening tests. However, many Type 2 diabetes patients have symptoms of polyuria and polydipsia. Type 2 diabetes patients have an abnormality of both, insulin resistance as well as β cells dysfunction. Although, initially, insulin is produced and do not require its therapy to sustain life, but eventually be required to control hyperglycemia and keep a normal level of HbA1C in 90% 0f patients. The metabolic variations in Type 2 are milder than of Type 1 because the absolute deficiency of insulin secretion in Type 1 diabetes leads to life-threatening ketoacidosis. Both types' Diagnosis is based most commonly on the presence of hyperglycemia that is, a fasting blood glucose concentration of equal to or greater than 126mg/dl. Pathogenesis does not involve viruses or autoimmune antibodies. An acute complication of Type 2 in the elderly is a hyperglycemic hyperosmolar state characterized by severe hyperglycemia and dehydration and altered mental status[4].

Since early 20s, The association of hyperuricemia with diabetes has been known, but the hypothesis that hyperuricemia is a risk factor for diabetes is still controversial. In fact, hyperuricemia was postulated to be the result of insulin resistance rather than its precursor5. However, many studies concluded that high serum uric acid has a strong association with risk of type 2 diabetes, independent of obesity, hypertension and, dyslipidemia. It has also been presumed in the development of diabetic nephropathy. Although some studies have demon¬strated the role of Uric Acid in the progression of pre-diabetes to dia¬betes, conflicting data exist about the uric acid levels in Type 2 DM, which are associated with risk factors and complications. Thus, the role of Uric Acid in the pathogenesis and the development of diabetic complications are debatable. Therefore, this study aimed to look for any association of serum uric acid with Diabetes Mellitus, while keeping the standard relevant clinical, biochemical and the anthropometric data.

MATERIALS AND METHODS

This is a Cross-sectional observational study was conducted in Population of Nowshera District KPK during the period January-December 2018. Nearly one hundred samples were collected from Qazi Hussain Ahmed Medical Complex on simple convenient method. A blood sample was drawn and brought to the Department of Biochemistry Laboratory of Nowshera Medical College Nowshera for further investigation of serum Uric Acid and Blood glucose level. Serum uric acid was estimated by enzymatic (uricase) method.

Their ages, smoking habits, physical status, and health conditions were recorded using a questionnaire. The study protocol was approved from the same institution ethical committee board. Informed consent of the subjects were taken. Diabetes was defined according to the guidelines of the American Diabetes Association (fasting serum glucose ≥126 mg/dL, random serum glucose ≥200 mg/dL). The age group selected for the study was 35-70 years.

Type 2 diabetes mellitus with complications were excluded from the study: those with blood and renal disorders, patients with a history of gout or on antihypertensive drugs, On long-term diuretics and steroids, antimetabolite and chemotherapy drugs, hypertension, arthritis, myocardial infarction or Hepatic disorders, Peripheral vascular disease, cerebrovascular disease, pulmonary tuberculosis, Renal transplant patients, Pregnancy and lactating mothers were excluded.

Data were analyzed using SPSS statistical software (version 22, SPSS). Data were expressed as mean±SD. Student's t-test was used to compare and asses the significance between groups. P-value < 0.05 was considered statistically significant.

Following steps were followed in serum uric acid estimation:

- Three test tubes were taken and marked as T.S and B.
- 1 ml Reagent was added in all three test tubes 1 ml each.
- 10 micro liter Serum was added in T marked tube.
- 10 micro liters' standard solution was added in S tube
- 10 micro liter distilled water was added in B tube
- All three tubes were mixed and incubated at the body temperature (37 C) for 5 min.
- Reading of absorbance against the reagent blank obtained on the Spectrophotometer at 546nm wavelength.
- Readings were calibrated with the slandered/ calibrator.
- Calculations were done according to the standard formula.

Uric acid [mg/dl] = Absorbance of sample ×6 Absorbance of standard

Following steps were followed in blood glucose estimation:

- Three test tubes were taken and marked as T, S, and B.
- 1 ml reagent was added in all three test tubes 1 ml each.
- 10 micro liter serums were added in T marked tube.
- 10 micro liter slandered solution was added in S

tube

- 10 micro liter distilled water was added in B tube
- All three tubes were mixed.
- Incubated at 37oC for 10 minutes.
- Reading of absorbance against the reagent blank obtained on the spectrophotometer at 546nm wavelength.
- Readings were calibrated with the standard/ calibrator.
- Calculations were done according to the standard formula.

Glucose [mg/dl] = Absorbance of sample × 100

Absorbance of standard

RESULTS

A blood sample of 100 selected patients was taken from patients visiting Qazi Hussain Ahmed Medical Complex Nowshera and brought to Department of Biochemistry Laboratory of Nowshera Medical College Nowshera to determine the Uric Acid and fasting and random blood glucose level and to know the relationship of Abnormal Uric Acid with Diabetic and Non-diabetic patients.

Mean age of the patients was 43.89±10-412 ranging from 24 to 65 years and mean Uric Acid was 5.628±1.069 ranging from 4.00 to 8.90 and mean blood glucose was 150.55±78.60 ranging from 89 to 443 as shown in Table 1.

According to the frequency of gender of the patients, Male patients were 39% while the Female patients were 61% out of 100 patients as shown in Table 2.

According to the frequency of diabetic patients, 24% patients had abnormal uric acid while the other 76% were normal uric acid out of the total 100 patients as shown in Table 3.

According to the history of Diabetic patients, 77% were non-diabetic patients, and 23% were diabetic out of the total 100 patients as shown in Table 4.

According to the cross tabulation, the number of cases having no diabetes were 77% out of which 59% of the patient had normal uric acid while 18% of the patient had abnormal uric acid. The number of cases having diabetes was 23% out of which 17% of the patients had normal uric acid while 6% of the patients had abnormal uric acid as shown in Table 5.

DISCUSSION

A blood sample of 100 selected patients were collected from patients visiting Qazi Hussain Ahmed Medical Complex Blood to determine the Uric Acid and fasting and random blood glucose level and to know the relationship of Abnormal Uric Acid with Diabetic and Non-diabetic patients.

The numbers of cases having no diabetes were 77% out of which 59% of the patient had normal uric acid while 18% of the patient had abnormal uric acid. The number of cases having diabetes was 23% out of which 17% of the patients had normal uric acid while 6% of the patients had abnormal uric acid

Uric acid is the end product of the purine metabolism in humans. IN urin acid production, The final two reactions i.e. the conversion of hypoxanthine to xanthine and then to uric acid, are catalyzed by the enzyme xanthine oxidoreductase, this enzyme persists in 2 inter-convertible forms, xanthine dehydrogenase or xanthine oxidase. The xanthine oxidase utilizes molecular oxygen as an electron acceptor and it generates a superoxide anion and other Reactive Oxygen Species (ROS), thus favoring an antioxidant pro-oxidant urate redox shuttle[6,7]. Uric Acid is also a physiological free radical scavenger and one of the major contributors of the plasma antioxidant capacity[8]. Thus, Uric Acid

Table 1: Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age (in years)	100	24	65	43.89	10.412
Diabetes	100	89	443	150.55	78.106
Uric Acid	100	4.00	8.90	5.6280	1.06951

Table 2: Frequency of Gender of the Patients

	Frequency	Percent
Male	39	39.0
Female	61	61.0
Total	100	100.0

Table 3: Frequency of Uric Acid Patients

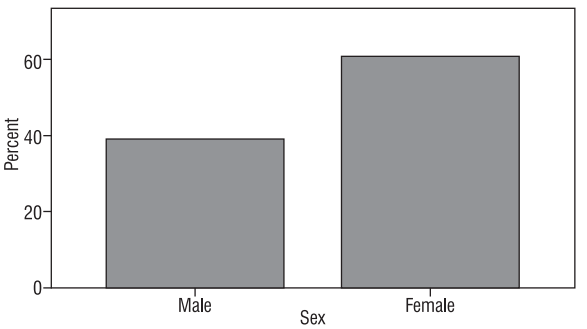
	Frequency	Percent
Normal	76	76.0
Abnormal	24	24.0
Total	100	100.0

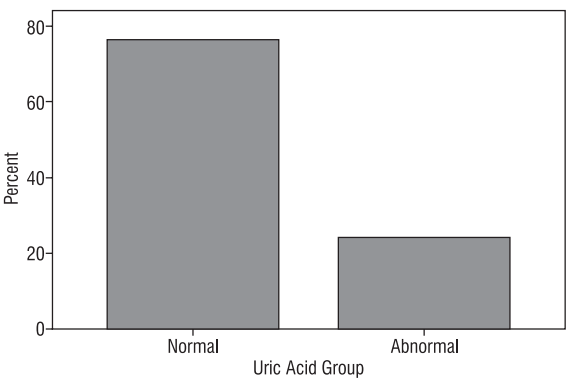
Table 4: Frequency of Diabetic Patients

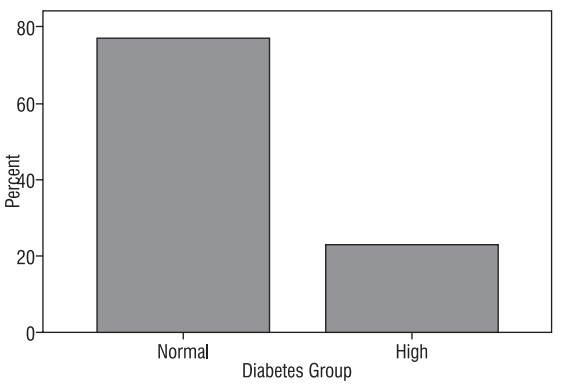
	Frequency	Percent
Normal	77	77.0
High	23	23.0
Total	100	100.0

Table 5: Cross Tabulation of Uric Acid with Diabetes

		Uric Acid Group		Total
		Normal	Abnormal	
	Normal Percentage	59	18	77
		59.0%	18.0%	77.0%
	High Percentage	17	6	23
		17.0%	6.0%	23.0%
Total		76	24	100
		76.0%	24.0%	100.0%
Chi-Square		0.789		
Pearson's R		0.792		







plays a dual role, both as a prooxidant and as an antioxidant[9,10]. Type 2 DM is associated with oxidative stress and increased free radical formation[11]. It is the hyperglycemia which generates free radicals and also impairs the endogenous antioxidant defense system[12]. Due to increased oxidative stress, local antioxidants are depleted and resulting in reducing the total antioxidant pool of the body[13]. Many studies have revealed the association of hypouricemia with Type 2 DM[14,15]. A positive relationship has been explained between glycosuria and uricosuria[16].

Further, a higher degree of hyper-glycemia was observed to be associated with an increased rate of uric acid clearance and lowering of the plasma uric acid levels[17]. Hypo-uricaemia and the tubular transport of uric acid have been thoroughly reviewed[18]. A greater urate clearance due to marked-up glomerular hyper-filtration which is a result of an abnormality in the tubular urate handling has been reported[19].

CONCLUSION

According to our study regarding the history of Diabetic patients, 77% were non-diabetic patients, and 23% were diabetic out of the total 100 patients as shown in Table 4. According to the cross tabulation, the number of cases having no diabetes were 77% out of which 59% of the patient had normal uric acid while 18% of the patient had abnormal uric acid.

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