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Original Research Article

Comparison of Serum Uric Acid in Normal, Prediabetic and Diabetic Subject.

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Conflict of interest: Nil

Abstract:

Objectives: This present study was to estimate and compare the serum uric acid in normal, prediabetic and diabetic person.

Methods: Glucose estimation was done by glucose oxidase peroxidase method by fully automatic analyser in Biochemistry unit of central laboratory in BMIMS Pawapuri, Nalanda. Uric acid is first oxidised to allantoin by uricase with the production of H_2O_2.The peroxide then react with 4-aminoantipyrene (4-AAP) and DHBS in presence of peroxidase to yield quinonimine dye. And then optical density was measured at 505 nm.

Result: In normal person mean fasting blood glucose with standard deviations were 85±9 mg/dl and mean post parandial blood glucose level with standard deviations were 100±11 mg/dl. In normal person mean serum uric acid level with standard deviation were 4.52±1.75 mg/dl. In prediabetic person mean fasting blood glucose level with standard deviation were 113±18 mg/dl and mean post parandial blood glucose with standard deviation were 173±18 mg/dl. serum uric acid with standard deviation in prediabetic person were 3.34±.79 mg/dl and p-value was less than 0.0002 with respect to normal person.

Conclusions: The serum uric acid was significantly decreased in uncomplicated prediabetic and diabetic person compared to normal person. In prediabetic this is due to utilisation of uric acid by oxidative stress in the body. In diabetic this is due to both oxidative stress and polyuria due to poor glycaemic control.

Keywords: Prediabetic, Diabetic, Serum uric acid

Introduction

Type 2 diabetes mellitus is chronic condition in which impairment of body to use and regulate glucose as fuel result in chronic hyperglycemia. Impairment in utilisation of glucose result from two process [1] Muscle and adipose tissue become resistance to insulin [2] Pancreas unable to produce enough insulin. India has about 77 million of people are suffering from diabetes mellitus, which make it second more affected after china [1].One in every six people with diabetes mellitus are in India [2]. Number will increase to 134 million by 2045 if not controlled as per international diabetes federation [2].

Uric acid is heterocyclic compound of C, H, O and N, is product of endogenous and exogenous purine catabolism. It is excreted through kidney. Uric acid is strong reducing agent and potent antioxidant at normal concentration of serum uric acid. Approximately half of the antioxidant property is duo to hydrogen urate ion [4]. The normal concentration of SUA in plasma is 2.5-8 mg in male and 1.5-6 mg /dl in female [5]. Normal excretion of uric acid 250 to 750 mg /day.

Hyperuricemia is a common condition estimated to occur in about 8.9 to 24.4 % of population [5,6]. In about 10% of cases hyperuricemia is primary, show familial incidence due to defect in enzyme of purine metabolism. Remaining cases are secondary due to increase turnover or reduced excretion. Increase serum uric acid may cause tissue damage over prolong period and increases the risk of type 2 diabetes mellitus, cardiovascular disease, metabolic syndrome etc due to prooxidant and proinflammatory action [5,7]. Hypouricemia is defined as SUA level less than 2 mg per dl.8. Possible cause of Hypouricemia include malignancy, diabetes mellitus, medication etc.

The relation between serum uric acid and diabetes mellitus is controversial. Some found increase serum uric acid levels in diabetes mellitus [9-14]. This is probably due to oxidative stress in diabetes mellitus. Due to hyperglycemia free radicals such as hydroxy radicals, super oxide ion are produced and uric acid produced as defence mechanism as urate is antioxidant at normal concentration of plasma and scavenge these radicals. High SUA in diabetes is also duo to insulin resistance and obesity in diabetes. There may also be Hypouricemia in diabetes mellitus [15,16]. This is due to increase renal clearance of uric acid [17,18]. Hypouricemia is usually associated with poor glycemic control and late onset kidney disease [17]. This present study was to estimate and compare the serum uric acid in normal, prediabetic and diabetic person.

Material & Methods

Estimation of serum uric acid in normal, prediabetic and diabetic person was done at Biochemistry unit of Central laboratory of BMIMS, Pawapuri, Nalanda. Permission was taken from ethical committee of BMIMS Pawapuri, Nalanda.

Selection of case: Total of 120 cases of different age and sex were selected out of which 40 were normal, 40 were prediabetic and 40 were diabetic. Person having fasting glucose 70mg/dl-100mg/dl and pp glucose less than 140 mg/dl were considered normal. Person having fasting glucose 100mg/dl -126 mg/dl and pp blood glucose less than 200mg/dl were considered prediabetic. Person having fasting blood glucose above 126 mg /dl and pp blood glucose above 200 mg /dl for more than two separate occasions were considered diabetic. Fasting blood samples were taken 8 hours after fast. Post parendial sample were 2 hours after meal. Glucose estimation was done by glucose oxidase peroxidase method by fully automatic analyser in Biochemistry unit of central laboratory in BMIMS Pawapuri, Nalanda.

Procedure: Venous blood was collected from antecubital vein in fluoride vial.

Principle: Glucose is oxidised to gluconic acid and hydrogen peroxide in presence of glucose oxidase. Hydrogen peroxide then react with 4-aminoantipyrene and 0-hydroxybenzoic acid to form red colour compound, and intensity of red colour was measured at 505 nm wavelength.

Reagent 1- enzyme reagent

Reagent 2- glucose standard 100mg/dl.

Three clean dry test tube was taken and labelled Blank(B), Standard (S) and Test(T)

Addition sequence	B	S	T
Enzyme reagent	1ml	1ml	1ml
Standard		10 micro litres	
Sample			10micro litre

Mixed and incubated at 37°C for 10 minutes. Absorbance of S and T was measured again reagent blank. Whole, procedure was automated in fully automatic analyser. Uric acid estimation was done by uricase method.

Principle:

Uric acid is first oxidised to allantoin by uricase with the production of H_2O_2.The peroxide then react with 4-aminoantipyrene (4-AAP) and DHBS in presence of peroxidase to yield quinonimine dye. And then optical density was measured at 505 nm.

Reagent 1- uric acid enzymes reagent.

Reagent 2- uric acid standard.

Procedure

Addition sequence	Reagent blank	Standard	Sample
Reagent 1	1000 micro litre	1000 micro litre	1000 micro litre
Standard		25 micro litre	
Sample			25 micro litre
Distilled water	25 micro litre		

Mix and incubate for 5 minutes at 37 °C. Measure optical density of Sample, Standard against reagent blank at 505 nm wavelength.

Calculation:

Uric acid (mg/dl) = OD of Sample/O D of standard × concentration of standard. Whole process was automated in fully automatic analyser. Serum urea, creatinine levels were also measured. Urine was examined for proteinuria.

Statistical Analysis

Data was analysed by using the MedCalc software. Mean and standard deviations were observed. Regression analysis was used. P value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Observations

Table 1: Sex wise distribution of prediabetic and diabetic patients

	Normal(n-40)		Prediabetic(n-40)		Diabetic(n-40)	
	Male (n-21)	Female (n-19)	Male (n-21)	Female (n-19)	Male (n-21)	Female (n-20)
SUA (mg/dl)	5.01±1.28	3.95±0.88	3.54±0.79	3.12±0.80	3.03±1.15	2.89±0.60
FBG (mg/dl)	88.05±8.08	82.78±8.40	112.75±18	112.47±17.45	190±65	197±68
PPBG (mg/d)	102.43±0.92	95.7±10.94	173.18±18	173.84±18.20	341±118	342±86

Table 2: Parameter of normal and diabetic patients.

	Normal	Diabetic	p-value
SUA(mg/dl)	4.51±1.75	2.96±.98	
FBG(mg/dl)	85±9	201±69	P<0.0001 significant
PPBG(mg/dl)	100±11	339±99	

Table 3: Parameter of normal and prediabetic patients.

	Normal(n-40)	Prediabetic(n-40)	
SUA(mg/dl)	4.51±1.75	3.34±0.79	P<0.0002
FBG(mg/dl)	85±9	113±18	
PPBG(mg/dl)	100±11	173±18	

Table 4: Parameter of diabetic and prediabetic patients.

	Diabetic (n-40)	Prediabetic (n-40)	
SUA(mg/dl)	2.96±0.98	3.34±0.79	P=0.0599 nonsignificant
FBG(mg/dl)	201±69	113±18	
PPBG(mg/dl)	339±39	173±18	

Table 5: Parameter of normal, prediabetic and diabetic patients.

	Normal(n-40)	Prediabetic (n-40)	Diabetic (n-40)
SUA(mg/dl)	4.51±1.75	3.34±0.79	2.96±0.98
FBG(mg/dl)	85±9	113±18	201±69
PPBG(mg/dl)	101±11	173±18	339±39

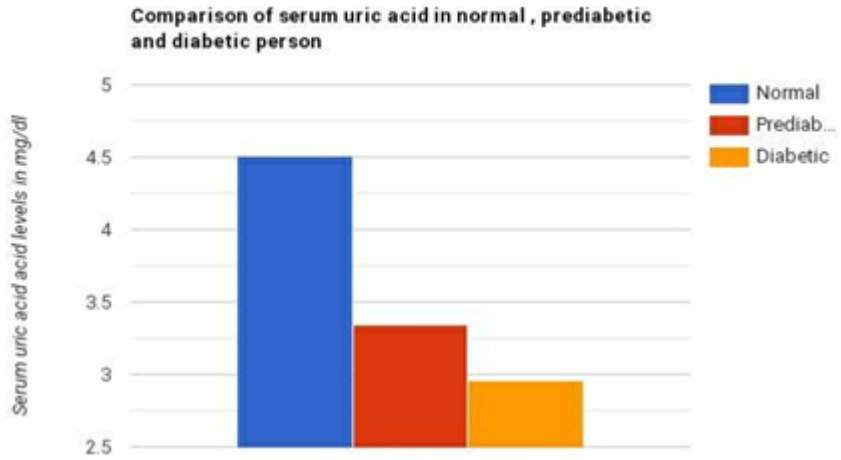

Figure 1: Comparison of serum uric acid in normal, prediabetic and diabetic cases.

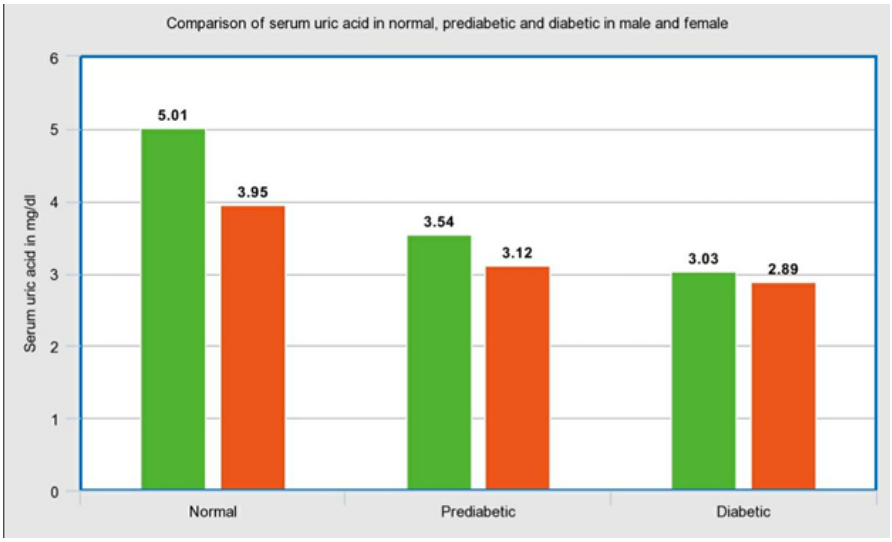

Figure 2: Comparison of serum uric acid in normal, prediabetic and diabetic cases.

The above tables shows comparison of serum uric acid in normal, prediabetic and diabetic person. In normal person mean fasting blood glucose with standard deviations were 85±9 mg/dl and mean post parandial blood glucose level with standard deviations were 100±11 mg/dl. In normal person mean serum uric acid level with standard deviation were 4.52±1.75 mg/dl. In prediabetic person mean fasting blood glucose level with standard deviation were 113±18 mg/dl and mean post parandial blood glucose with standard deviation were 173±18 mg/dl serum uric acid with standard deviation in prediabetic person were 3.34±.79 mg/dl and p-value was less than 0.0002 with respect to normal person as shown in table 3, fig-1 and 2. In diabetic person. In diabetic person mean fasting blood glucose level with standard deviation were 201±69 mg/dl and post parandial blood glucose with standard deviation were 339±39 mg/dl. Mean Serum uric acid level with standard deviation in diabetic person were 2.96±0.98 mg/dl with p-value <0.0001 from normal person which was more than 0.05 and was significant decrease in uric acid in diabetic person than normal person as shown in table-2 and figure-1 and 2. There was slightly less serum uric acid levels in female in normal, prediabetic and diabetic person which was non-significant.

Discussions

Our study shows comparison of serum uric acid in normal, prediabetic and diabetic person. There was significant decrease in serum uric acid in prediabetic and diabetic person from normal person. Female had slightly lower serum uric acid than male in all group. Low serum uric acid in diabetic and prediabetic person was seen by many author previously. Tanqigel Haque seen inverse relationship between serum uric acid levels and diabetes mellitus. Herman J, Goldbourt and many other author [16] also found inverse relation between serum uric acid and diabetes mellitus. Nan H, Dong Y, Gao W [19] also found decreased serum uric acid when fasting plasma glucose above 150 mg/dl in Chinese people. The study of Gotoh and his friends [20] also give attention to relation between glycosuria and decreased serum uric acid. In other study low serum uric acid in diabetes is associated with hyper infiltrable kidney, poor metabolic control and late onset kidney disease.

According to our study and some previous study there is inverse relation between serum uric acid and diabetes mellitus. Most probable cause is glycosuria that leads to osmotic diuresis and more excretion of uric acid through kidney. In these studies hypouricemia increases as level of glycosuria increases and increase uric acid clearance by hyper infiltrable diabetic

kidney leads to hypouricemia. According to Memisogullari R, Yuksel HK, Coskun A. [21] serum uric acid was significantly decreased in diabetic person with normal kidney function than control group. According to study of Son and his friends 28.3% of hypouricemia associated with diabetes. Malignancy is most common cause of hypouricemia (43.4%).

Bugdayce and his colleagues [22] found 16% cases of hypouricemia is associated with diabetes. There is also molecular basis of glycosuria induced hypouricemia in diabetic person. vitart at. Al. reported role of GLUT 9 as uric acid transporter. Anazai et al reported GLUT 9 transporter is voltage driven transporter (RAT V1). This explains role of Glucose-uric acid interaction in excretion of uric acid through GLUT 9 transporter. [23] In diabetes mellitus there is oxidative stress. Uric acid has antioxidant property. Hypouricemia in diabetes mellitus is most probably due to utilisation of uric acid in scavenging free oxygen radicals.

Conclusions

This study concluded the serum uric acid was significantly decreased in uncomplicated prediabetic and diabetic person compared to normal person. In prediabetic this is due to utilisation of uric acid by oxidative stress in the body. In diabetic this is due to both oxidative stress and polyuria due to poor glycaemic control.

Limitations: This present study was case-control and hospital-based study. various researchers studied Serum uric acid in diabetes mellitus time to time, they found contversial result. our study was small effort to compare serum uric acid in normal, prediabetic and diabetic person. Continuous study is needed for more information.

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