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(RESEARCH ARTICLE)



Serum uric acid level among diabetic, hypertensive and diabetic-hypertensive patients attending specialist hospital Sokoto

Yale Bala Malam ^{1,*}, Yeldu Muhammed Haruna ¹, Dallatu Kabiru Muhammed ¹ and Danjuma Abubakar ²¹ Department of Chemical Pathology, School of Medical Laboratory Sciences, Usmanu Danfodiyo University, PMB 2346, Sokoto, Nigeria.² Department of Chemical Pathology, Federal Medical Center Bida, Niger State, Nigeria.

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Abstract

Elevated serum uric acid is associated with metabolic disorders such as insulin resistance, hypertension, diabetes, dyslipidaemia and also increases the risk of cardiovascular disease. This study evaluated serum uric acid and fasting plasma glucose in diabetic, hypertensive and diabetic-hypertensive patients. This study consist of 120 subjects including 30 diabetics, 30 hypertensives, 30 diabetic-hypertensive patients and 30 age- and sex-matched controls. The mean serum uric acid was significantly ($p < 0.001$) higher in diabetic, hypertensive and diabetic-hypertensive patients when compared with those of controls. While the mean values of fasting plasma glucose were significantly ($p < 0.001$, $p = 0.007$ and $p < 0.001$) higher in diabetic, hypertensive and diabetic-hypertensive patients respectively when compared with those of controls. It was concluded from the finding of this study that, serum uric acid level and fasting plasma glucose increases significantly in diabetic, hypertensive and diabetic-hypertensive patients. It is recommended that serum uric acid and plasma glucose should be included as a routine investigation for the management of these groups of individuals to avoid the risk of cardiovascular diseases.

Keywords: Uric acid; Glucose; Hypertension; Diabetes; Patients; Controls

1. Introduction

Diabetes mellitus is a metabolic disorder characterized by the presence of chronic hyperglycaemia accompanied by greater or lesser impairment in the metabolism of carbohydrate, lipids and proteins [1]. The prevalence of diabetes in Nigeria is 4-10% [2]. In Sokoto, the reported prevalence of diabetes is 6.0% [3]. Three types of diabetes mellitus exist; type 1 which results from the failure of the pancreas to produce insulin, type 2 which results from an inability of the body to use insulin optimally and gestational diabetes which occurs in pregnant women without a previous diagnosis of diabetes [4].

Hypertension is a sustained elevation of resting systolic blood pressure (BP) ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg or both [5]. It is divided into primary and secondary according to whether the cause is known or unknown [6]. Secondary hypertension is the one in which the cause is known, it is more common in children and occurs in less than 5% of people living with hypertension [6]. Kidney and vascular diseases are the most common causes of secondary hypertension. Primary; formerly referred to as essential hypertension is the one in which the cause is unknown and it is the most common, which occurs in over 95% of people living with hypertension [6]. The reported prevalence of hypertension varies around the world, with the lowest prevalence in rural India (3.4% in men and 6.8% in women) and highest in Poland (68.9% in men and 73.5% in women) [7]. About 85% of uric acid is synthesized in our body and only 15% is by

* Corresponding author

E-mail address: yalebala@gmail.com

food intake. Hyperuricaemia can result from increased urate production, decreased uric acid excretion by the kidneys, or a combination of the two mechanisms. Serum uric acid level can be a strong predictor of cardiovascular disease when combined with elevated blood pressure (even mildly elevated) [8]. Endothelial dysfunction may be a possible pathway linking uric acid and cardiovascular disease [8]. Uric acid is thought to play a pathogenic role in hypertension mediated by several mechanisms such as inflammation, vascular smooth muscle cell proliferation in renal microcirculation, endothelial dysfunction and activation of the renin-angiotensin-aldosterone system [9].

2. Material and methods

2.1. Study area

The study was carried out at specialist hospital Sokoto. Sokoto state is located at the extreme part of north-western Nigeria between longitude 3° and 7° east and between latitude 10° and 14° north of the equator. It shares borders with Niger-republic to the north, Kebbi state to the south-west and Zamfara State to the east [10]. The state covers a total land area of about 32,000 square kilometers and a population of 4,602,298 million based on the 2013 projection [11]. Sokoto state has semi-arid climate and vegetation is largely Sudan savannah with annual rainfall between 500 – 1300 mm and a temperature range between 15°C and over 40°C during warm days [10]. The indigenous inhabitant of the area is mainly Hausa and Fulani. Other ethnic groups resident in the area include Igbo, Nupe, Ibra, Igala etc. Hausa is the most spoken language. Traders and farmers form the greater part of this population, while there are civil servants, artisans and people of other occupational callings [12].

2.2. Study population

A total of 120 subjects were used for this study. This consists of 30 diabetic, 30 hypertensives, 30 diabetic-hypertensive and 30 control subjects attending specialist hospital Sokoto. The subject selection and clinical examination were performed by the consultant physicians in the clinic. In all the patients and controls, informed consent was obtained from each prior to the commencement of the study.

2.3. Study design

This is a cross-sectional study. At enrolment, a structured study questionnaire was used to elicit the subject demographic and socioeconomic data such as age, sex, marital status, occupation, present of any disease, family history among others.

The subjects were classified into the following groups:-

GROUP A: Diabetic patients (n =30).

GROUP B: Hypertensive patients (n =30)

GROUP C: Diabetic-hypertensive patients (n =30)

GROUP D: Control subjects (n =30).

2.4. Sample size determination

The sample size for the study was calculated using the standard formula below [13].

$$n = \frac{(z^2pq)}{d^2}$$

Where:

n = Number of the sample, for a population greater than 10,000, Z = Standard normal deviation, usually set at 1.96, which corresponds to the 95% confidence level, P = Prevalence rate of diabetes in Sokoto which is 6.0% [3]. q = complement of p, which is 1-p, d = Degree of accuracy desired, usually set at 0.05.

Therefore the minimum sample size was calculated as follow:

$$n = \frac{(1.96)^2(0.06)(1-0.06)}{(0.05)^2}$$

$$n = \frac{3.8416 \times 0.06 \times 0.94}{0.0025}$$

$$n = \frac{0.21666624}{0.0025}$$

$$n = 86.666 \approx 87$$

The calculated sample size is 87.

2.5. Ethical consideration

Ethical approval of the study was obtained from the ethical and research committee of specialist hospital Sokoto, in accordance with the Helsinki. Informed consent was obtained from the participants enrolled in the research.

2.6. Sampling techniques

2.6.1. Subject selection

A convenient sampling technique was used to recruit the subjects until the desired sample-sized attained. In all the groups, at respective locations, subject selection, clinical examination and anthropometric measurements were carried out by consultant physicians. Written informed consent was obtained from each subject prior to the recruitment.

2.6.2. Blood sample collection and processing

Three (3) milliliters of venous blood was collected via venipuncture using a vacutainer syringe after an overnight fast of at least eight to ten hours from all the participants. One and a half milliliter was dispensed into a plane sterile vacutainer and fluoride oxalate tubes. The plain samples were allowed to clot and centrifuged at 4000 rpm for 5 minutes. The sera obtained was rapidly harvested and stored at -20°C until the analysis time. While plasma was obtained from the anti-coagulated samples after centrifugation.

2.7. Measurement of blood pressure

Blood pressure measurement was carried out by the consultant physician using manual blood pressure apparatus (sphygmomanometer and stethoscope) applied to a bared upper arm supported at the level of the heart with the individual in a relaxed mood. The brachial artery was partially occluded by inflating the blood pressure apparatus. The apparatus was then deflated until the pressure is low enough to allow blood to start flowing into the arm. The resumption of blood flow in the underline brachial artery generates turbulence that produces sound (Korotkoff sounds). The pressure corresponding to the beginning of blood flow (first Korotkoff sound) is the highest pressure in the artery and was detected using a stethoscope placed over the artery just below the cuff. This is called systolic blood pressure. The pressure corresponding to the disappearance of turbulence (the lowest pressure in the artery) is called diastolic pressure [14].

2.8. Anthropometric measurement

2.8.1. Weight

The weight was measured using an electronic balance beam scale. The subjects were weight with light clothes and no shoes. The weight was then read according to human resources and services administration to the nearest 0.1 kg [15].

2.8.2. Height

The subject stands erect and via footed on a Stadiometer. The height was read and recorded to the nearest 0.5 cm [15].

2.8.3. Body mass index (BMI)

The body mass index was calculated using the formula as follows:

$$\text{BMI} = \frac{\text{Weight in kg}}{\text{Height in m}^2}$$

Height in m²

2.9. Laboratory analytical methods

2.9.1. Estimation of serum uric acid

This was based on the enzymatic colorimetric method described by Fossati *et al.*, [16] using the reagent kit (LAB KIT Ltd, India).

2.9.2. Estimation of plasma glucose

This was based on the enzymatic colorimetric method described by Trinder [17] using the reagent kit (Agappe Diagnostics Ltd, India) for the assay.

2.10. Statistical analysis

The data generated were analyzed using the statistical package for social sciences (SPSS) version 23. The results of serum uric acid, fasting plasma glucose, blood pressure and anthropometric parameters were analyzed and expressed as mean plus/minus standard error of the mean (mean±SEM). The results of both the clinical and biochemical parameters were compared between different groups using a one-way analysis of variance (ANOVA) for matched samples. A p-value of less than 0.05 (p< 0.05) was considered significant.

3. Results

Table 1 shows age and gender distribution of diabetic, hypertensive, diabetic-hypertensive patients and controls in their different age classes. A total of 30 diabetics (16 males and 14 females), 30 hypertensives (13 males and 17 females) and diabetic-hypertensive (6 males and 24 females) patients were recruited. A total of 30 apparently healthy subjects were recruited (20 males and 10 females) as controls. Most of the subjects were within the age range of 47-60 years.

Table 1 Age (years) and Gender Distribution of the Study Population

Age class	DM		HTN		D-H		C		Total
	M (n=16)	F (n=14)	M (n=13)	F (n=17)	M (n=6)	F (n=24)	M (n=20)	F (n=10)	
18-32	2	3	1	1	5	4	10	8	34
33-46	2	3	2	3	1	10	1	2	24
47-60	11	8	10	9	5	10	4	5	62
Total	15	14	13	13	11	24	15	15	120

DM= Diabetic; HTN= Hypertensive; D-H= Diabetic-hypertensive; n= Number of subject; C= Control; M= Male; F= Female.

Table 2 shows the results of the demographic characteristics of the study population. The results show that 64.2% of the subjects were married, 70% were predominantly Hausas and 65% were on medications.

Table 2 Demographic Characteristics of the Study Population

Characteristics	No. of Subjects (n=120)	Percentage (100%)
Marital Status		
Married	77	64.2
Single	37	30.8
Divorced	6	5
Ethnic Group		
Hausa	84	70
Fulani	18	15
Yoruba	3	2.5
Igbo	3	2.5
Others	12	10
Occupation		
Students	25	20.8
Civil Servant	13	10.8
Others	82	68.3
Medication		
Yes	78	63
No	42	35

Table 3 shows serum uric acid and fasting plasma glucose in diabetic, hypertensive, diabetic-hypertensive patients and controls. The mean values of serum uric acid were significantly ($p < 0.001$) higher in diabetic, hypertensive and diabetic-hypertensive patients when compared with controls. Also, the mean values of fasting plasma glucose concentration in diabetic, hypertensive and diabetic-hypertensive patients were significantly ($p < 0.001$, $p = 0.007$ and $p < 0.001$ respectively) higher when compared with those of controls.

Table 3 Serum Uric Acid and Fasting Plasma Glucose Level of the Study Population

GROUP	N	SUA (mg/dL)	FPG (mmol/L)
1	30	5.48±0.23	10.30±0.73
2	30	5.95±0.30	6.53±0.38
3	30	5.44±0.29	7.61±0.41
4	30	3.27±0.06	4.36±0.10
P-value		<0.001	<0.001
Post hoc Test			
Group 1 Vs 4		P<0.001	P<0.001
Group 2 Vs 4		P<0.001	P= 0.007
Group 3 Vs 4		P<0.001	P<0.001
Group 1 Vs 2		P= 0.517	P<0.001
Group 1 Vs 3		P= 0.999	P<0.001
Group 2 Vs 3		P= 0.445	P= 0.003

Values are mean± SEM; n= Number of subjects; SUA= Serum uric acid; FPG= Fasting plasma glucose; 1= Diabetic 2= Hypertensive; 3= Diabetic-hypertensive; 4= Controls.

Table 4 shows the mean values of BMI and blood pressure in diabetic, hypertensive, diabetic-hypertensive patients and controls. The mean values of BMI were significantly ($p = 0.023$) higher in diabetic-hypertensive patients as compared

with those of controls, also the mean values of SBP were significantly ($p < 0.001$) higher in hypertensive patients as compared with those of controls.

Table 4 Anthropometric parameters and Blood Pressure of the Study Population

Group	W (kg)	H (m ²)	BMI (kg/m ²)	SBP (mmHg)	DBP (mmHg)
1	63.93±2.59	1.65±0.02	23.62±0.98	137.53±3.35	84.13±2.69
2	68.83±3.04	1.64±0.01	25.54±1.10	158.37±4.71	96.97±2.83
3	68.40±2.51	1.61±0.01	26.19±0.87	144.97±4.47	91.40±3.11
4	60.50±1.25	1.62±0.02	22.50±0.59	125.97±3.74	88.10±0.65
P-value	0.012	0.218	0.060	<0.001	0.004
Post hoc Test					
G 1 Vs 4	p= 0.752	p= 0.677	p= 0.814	p= 0.197	p= 0.681
G 2 Vs 4	p= 0.080	p= 0.815	P= 0.086	p<0.001	p= 0.067
G 3 Vs 4	p= 0.106	p= 0.976	p= 0.023	p= 0.008	p= 0.790
G 1 Vs 2	p= 0.489	p= 0.995	p= 0.439	p= 0.003	p= 0.003
G 1 Vs 3	p= 0.568	p= 0.418	p= 0.191	p= 0.577	p= 0.179
G 2 Vs 3	p= 0.999	p= 0.566	p= 0.958	p= 0.102	p= 0.403

Values are mean± SEM; H= Height; W= Weight; BMI= Body mass index; SBP= Systolic blood pressure; DBP= Diastolic blood pressure; G= Group; VS= versus; 1= Diabetic 2= Hypertensive; 3= Diabetic-hypertensive; 4= Controls.

4. Discussion

Uric acid is a ubiquitous byproduct of purine metabolism in humans and higher primates, Hyperuricaemia has been associated with hypertension, diabetes mellitus, and metabolic syndromes and even increase the risk of cardiovascular diseases [18].

The current study demonstrated that most of the study subjects are Hausas (70%) and the majority of them are married (64.2%). Most of them are within the age range of 47-60, and about 78 (65%) were on medications.

The finding of significant ($p < 0.001$) increase in serum uric acid among diabetic, hypertensive and diabetic-hypertensive patients as compared with controls, agreed with the previous studies of Babikr *et al.*, [19] and Venkateswara and Vanukuri, [20]. This could be due to the effect of insulin which may stimulate sodium and urate reabsorption in the proximal tubule which leads to increase serum uric acid level. The increase in the level of uric acid in this patient may be due to the diuretic activity of some drugs in which the patients used for their treatment.

Increased serum uric acid was reported in subjects with obesity, insulin resistance, and dyslipidaemia. Hyperuricaemia frequently occurs because insulin stimulates sodium and urate reabsorption in the proximal tubule [21]. The uric acid level is increased in subjects with renal disease as a result of decreased glomerular filtration rate (GFR) and renal urate excretion [22]. Diuretics increase serum uric acid but the clinical relevance of these effects remains uncertain [23]. It has been suggested that the increase in serum uric acid caused by diuretic treatment may partially offset the benefits of blood pressure reduction [24].

Uric acid causes hypertension in a rat model through the activation of the renin-angiotensin system, down-regulation of nitric oxide, and induction of endothelial dysfunction and vascular smooth muscle proliferation [25]. Uric acid is thought to play a role in hypertension mediated by several mechanisms such as inflammation, vascular smooth muscle cell proliferation in renal microcirculation, endothelial dysfunction and activation of the renin-angiotensin-aldosterone system [26].

The finding of significant ($p < 0.001$, $p = 0.007$, $p < 0.001$) increased in fasting plasma glucose of diabetic, hypertensive and diabetic-hypertensive patients respectively, as compared to those of controls is consistent with the report of [27]; [19];

[20]. The hyperglycaemia may be due to stress, ageing and an imbalance of glucose production from the non-carbohydrate source such as lipid, protein. Multiple factors in an older person contributed to such an imbalance of glucose regulation [28]. The hyperglycaemic condition may result due to insulin resistance, viral infection, inflammation and obesity [29].

The finding of significant ($p=0.023$) increased in BMI of diabetic-hypertensive patients as compared with those of controls agreed with the study of [30]. Similarly, the finding of significant ($p<0.001$) increased in SBP of hypertensive patients as compared with those of controls also agreed with the study of [30]. The increase in BMI may be a result of impaired glucose metabolism which results in lipogenesis hence increase the body mass, while the increased SBP may be a result of increased deposition of lipid most especially cholesterol along the blood vessels.

5. Conclusion

There was a significant increase in the mean of serum uric acid and fasting plasma glucose among diabetic, hypertensive and diabetic-hypertensive patients as compared with those of controls. Future studies should focus on evaluating the effect of hyperuricaemia as a risk factor for the development of cardiovascular disease in this group of patients.

Compliance with ethical standards

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Disclosure of conflict of interest

This article is not the object of any conflict of interest and has not been submitted to other journals for publication. Therefore, we authorize the journal to publish it.

Statement of ethical approval

Ethical approval of the study was obtained from the ethical and research committee of specialist hospital Sokoto.

Statement of informed consent

Informed consent was obtained from the participants enrolled in the research. The participants were fully informed about the research aim and their confidentiality was maintained.

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