European Journal of Clinical and Biomedical Sciences
2019; 5(2): 27-38
http://www.sciencepublishinggroup.com/j/ejcbs
doi: 10.11648/j.ejcbs.20190502.11
ISSN: 2575-4998 (Print); ISSN: 2575-5005 (Online)

Risk Factors for Undiagnosed Hyperuricemia and Gout: Influence of Personal Characteristics, Life Style and Cardio-Metabolic Status: A Cross Sectional Study

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To cite this article:

Christopher Edet Ekpenyong, Inyang Udoinyang Clement, Caleb Effiong Edet. Risk Factors for Undiagnosed Hyperuricemia and Gout: Influence of Personal Characteristics, Life Style and Cardio-Metabolic Status: A Cross Sectional Study. *European Journal of Clinical and Biomedical Sciences.* Vol. 5, No. 2, 2019, pp. 27-38. doi: 10.11648/j.ejcbs.20190502.11

Received: February 20, 2019; **Accepted**: March 25, 2019; **Published**: May 23, 2019

Abstract: Despite the increasing prevalence of hyperuricemia in the general population and its association with many diseases, serum uric acid (SUA) level has not been routinely determined in the evaluation and management of patients, especially those with metabolic disorders. This cross-sectional study used standard methods to assess the influence of personal characteristics, lifestyle and cardio-metabolic status on SUA levels of patients who visited a primary care center in Southern Nigeria. Forty-nine point seven percent of participants were hyperuricemic. Significant association and higher odds for hyperuricemia were found among participants who were married (Odd Ratio (OR)=2.24,95%Confidence interval (C.I) 1.947-5.303), dehydrated (OR=1.46,C.I 0.845-2.535), currently consuming alcohol (OR=5.199, C.I 4.249-69.623), with poor dietary habits (OR=1.23,C.I0.982-7.2356), physically inactive (OR=2.760,C.I 0.294-25.881), night clubbing (OR=3.09,C.I3.22-12.982), frequently drinking soft/sweet drinks (OR=3.42,C.I 2.01-10.29), abnormal anthropometric profile (OR=1.27,CI 1.094-1.485) for BMI and OR=1.52,C.I 0.874-2.656) for waist circumference) and metabolic disorders including hypertension (OR=1.60,C.I 1.280-2.008), T2DM (OR=1.27,C.I 1.089-1.474), dyslipidemia and musculoskeletal disorders (OR=3.26,C.I1.633-6.492). Demographic factors, poor lifestyle habits, abnormal adiposity and metabolic aberrations drive hyperuricemia and therefore underline the need for SUA evaluation and management among those with these characteristics to prevent associated diseases.

Keywords: Hyperuricemia, Lifestyle, Demographics, Dysmetabolic Syndrome

1. Introduction

Worldwide hyperuricemia is highly prevalent and affects all strata of the general population including the pre-school and school aged children and adults [1]. It is an independent risk factor for all cause mortality and cardiovascular disease mortality [2]. Serum uric acid (SUA) is a weak acid produced from the breakdown of purines in the body by enzymes called xanthine oxidases. About a third of SUA is synthesized from dietary purine while two thirds is produced endogenously in pathways catalyzed by a number of enzymes.

The kidney tightly regulates SUA level by regulating clearance, glomerular filtration, reabsorption, secretion and post-secretory absorption. It reabsorbs about 90-95% of the uric acid (UA) filtered at the glomeruli and excretes about 65-75% of UA produced daily through the actions of some urate transporters, while 25-35% is excreted by extra-renal routes. Deviation from the normal metabolic pathways results in hyperuricemia, a precursor for gout (UA crystals accumulation in joints and tissues causing inflammation and pain). Hyperuricemia is etiologically related to the over production or decreased excretion of UA by renal and extra-renal routes or a mixture of both. This abnormal UA metabolism could be genetically predisposed or acquired. Chronic hyperuricemia has been implicated in the pathogenesis of several metabolic disorders including hypertension, type2 diabetes mellitus (T2DM), dyslipidemia,

cardiovascular diseases, obesity, hyper-insulinemia, insulin resistance and renal diseases including renal stones.

One study [3] reported that hyperuricemia predicts cardiovascular events in the general population, the hypertensive population and increases the risk for future hypertension as well as worsening pre-existing CVD. Infact, there is a convincing evidence for a role of childhood hyperuricemia in hypertension in later life [4-6].

The link between hyperuricemia and metabolic disorders, the paucity of data reporting on the prevalence and associated risk factors in the general population, and in particular in developing countries underscore the need for studies evaluating the influence of personal characteristics, life style and cardio-metabolic status on SUA level in the general population which hitherto has not been documented in some developing countries such as Nigeria. The identification of risk factors for any disease is an important step for early prevention of the disease [7].

The aim of this study was to assess the influence of personal characteristics, lifestyle and cardio-metabolic status on SUA level of an adult population.

2. Materials and Methods

2.1. Subjects and Methods

The study enrolled 79 (42 males and 37 females) hyperuricemic and 80 (39 males and 41 females) age and sex-matched normouricemic subjects attending a primary care center in Uyo Southern Nigeria within the study period (January 2015 and August 2017). They were selected from an initial 270 respondents who were invited to participate after applying the inclusion/exclusion criteria. Exclusion criteria included age outside of the study range, decline participation, missing data and inadequate questionnaire responses. Written informed consent was obtained from all participants and the management of the health facility granted approval for the conduct of the study. For the purpose of this cross-sectional study, hyperuricemia was defined as SUA >6mg/dL for women and >7mg/dL for men [8]. The participants were informed that participation was voluntary and withdrawal from participation was allowed at any stage of the study.

2.2. Assessment Measures

Two instruments of survey were used to assess the participants who were classified as hyperuricemic and normouricemic. These included a semi-structured socio-demographic and medical history questionnaires adapted from previous studies on risk factors for hyperuricemia [9] and serum biochemical assay for biochemical markers of hyperuricemia including SUA level and associated markers of metabolic abberrations such as serum creatinine (SCr), lipid sub-fractions, and oxidative stress (OS) markers and markers of insulin resistance (IR).

The first section of the questionnaire contained 16 open-ended questions seeking to obtain information about the respondents' socio-demographic characteristics including age (years), gender, marital status, monthly income, educational level, occupation, alcohol consumption, dietary habits, coffee consumption, physical activity status, water intake, cigarette smoking status, seafood consumption, regular intake of soft/sweet drinks, yoghurt and milk consumption.

Age was stratified into 2 groups 18-35 years and >35 years. Marital status was classified into single, married, divorced and widow. Monthly income was grouped into 4 groups including < 10,000, 10,000-19,000, 20,000-30,000 and >30,000. Educational levels were classified into primary, secondary and tertiary education.

Alcohol intake particularly spirit and beer were enquired about and participants were stratified into current drinkers (those who drank up to 24hrs prior to commencement of the study), ex-drinkers (those who stopped drinking 6 months before study commenced) and non-drinkers (those who never drink alcohol).

Dietary habits were grouped into good (moderate intake of balanced diet 2-3 times a day with a substantial amount of fruit and vegetables) and poor (excessive consumption of unbalanced diets with little or no fruits and vegetables added to it). Information on nutrients intake and food groups (meat, dairy, seafood, coffee, yogurt and soft drink) was also obtained. Water intake was classified as adequate (intake of ≥ 3.7 L/24hr for men and ≥ 2.7 L/24hr for women). Intake of less than these amounts was regarded as inadequate intake for male and females respectively.

Physical activity status was assessed based on the 2010 US healthy people physical activity guidelines standards which recommends 150 minutes of moderate to severe intensity of aerobic exercise per week in bouts of 10 munities or more for adults ages between 18 and 64 years.

Cigarette smoking status was established by asking the participants whether they currently smoke, formally smoked or never smoked. Those who smoked on the day of the survey were defined as current smokers, those who had stopped smoking were classified as ex-smokers and those who never smoke were grouped as none-smokers.

2.3. Anthropometric Assessment

The body mass index (BMI) was calculated as the ratio of body weight in kilogram divided by the square of body height in meters.

Weight was measured with a digital scale to the nearest 0.1kg. A fixed stadiometer was used to measure height to the nearest 0.1cm. BMI < 18.5kg/m^2 was considered underweight, 18.5-24.9kg/m^2 normal weight, ≥ 25.0kg/m^2 was considered overweight while ≥ 30kg/m^2 was regarded as obese.

Waist circumference (WC) was measured at the iliac crest to the nearest mm with a soft non-elastic measurement tape. WC > 94cm and >80cm for men and women respectively were considered abnormal (indicative of central obesity) [10]

2.4. Assessment of Saerum Uric Acid and Other Components of Metabolic Syndrome

Blood pressure (BP) was measured after sitting quietly for

15 minute but before venous blood was drawn using a mercury sphygmomanometer (Acosin 300, Dekamet Ltd England) with the appropriate cuff size. Normotension was defined as a systolic BP < 140mmHg and diastolic BP< 90mmHg. Above these values BP was considered to be in hypertensive range [9].

2.5. Biochemical Analysis

About 5ml venous blood samples were collected from the antecubital veins of all participants after 12h of overnight fast in two specimen bottles, one containing ethylenediaminetetra acetic acid (EDTA) and another without EDTA for the determination of SUA levels, lipid sub-fractions, glucose, urea and Cr, using standard protocols). Serum insulin was measured by an enzyme-linked immunosorbent (ELISA) method using commercially available kit (Clouol-clone-corp, Houston USA).

Homeostasis model assessment-insulin resistance (HOMA-IR) was calculated as follows; HOMA-IR = [fasting glucose (mmol/L x fasting insulin (μIU/mol/22.5))]. HOMA-IR ≥ 1.8 indicates IR [11].

Fasting serum glucose (FBG) and lipid sub-fractions were measured using a multi-channel Automated System lipid pro TM Model KM-001A; info Pia Co Ltd. South Korea. SUA was measured by standard enzymatic colorimetric method [12].

Urinary specific gravity (USG) was measured using an electronic handled optical refractometer. USG > 1.020 was regarded as inadequate hydration (dehydration) while USG ≤ 1.020 was regarded as adequate hydration. Musculoskeletal disorders (MSDs) were defined as injuries/pains affecting muscle, tendons, joints, nerves, ligaments and blood vessels, and was classified according to body parts [13].

Diabetes mellitus (DM) was diagnosed as two fasting blood glucose (2FBG) levels of ≥7.0mmol/L or 126mgl/dL. two 2-h post prandial glucose (2hPPG) reading of 200mg/dL (11.1mmol/L) or higher after a glucose load of 75g. Two casual glucose readings of 200mg/dL (11.1mmol/L) or higher. Glycosylated hemoglobin (HbA/c) ≥ 6.5%. History of physician-diagnosed diabetes mellitus, or use of glucose lowering medication [14].

Table 1. *Socio-demographic characteristics of study participants.*

Socio-demographic variables of participants	Total (n=159)	Hyperuricemia (n=79)	Normouricemia (n=80)	X^2-value.	P-value
Gender					
Male	81 (50.9)	42 (53.2)	39 (48.8)	0.158	0.691
Female	78 (49.1)	37 (46.8)	41 (51.2)		
Age (yrs)					
≤ 35	59 (37.1)	23 (29.1)	36 (45.0)	3.65	0.056
> 35	56 (62.9)	56 (70.9)	44 (55.0)		
Marital status					
Single	42 (26.4)	12 (15.2)	30 (37.5)		
Married	89 (56.0)	53 (67.1)	36 (45.0)	12.25	0.007*
Divorced/separate	13 (8.2)	5 (6.3)	8 (10.0)		
Widowed	15 (9.4)	9 (11.4)	6 (7.5)		
Monthly income (Naira)					
< 10, 000	48 (30.2)	25 (31.6)	23 (28.7)		
10, 000-20,000	68 (42.8)	36 (45.6)	32 (40.0)	1.646	0.6490
20, 000-30,000	27 (17.0)	12 (15.2)	15 (18.8)		
> 30, 000	16 (10.1)	6 (7.6)	10 (12.5)		
Educational level					
Primary education	15 (9.6)	6 (7.9)	9 (11.3)		
Secondary education	115 (73.7)	58 (76.3)	57 (71.3)	0.660	0.719
Tertiary education	26 (16.7)	12 (15.8)	14 (17.5)		
Occupation					
Employed	31 (18.3)	13 (16.5)	18 (20.0)		
Unemployed	98 (58.0)	46 (58.2)	52 (57.8)	0.866	0.834
Retired	22 (13.0)	12 (15.2)	10 (11.1)		
Petty traders	18 (10.7)	8 (10.1)	10 (11.1)		

Significant at 5% ($p<0.05$)

Table 2. *Association between lifestyle habits and hyperuricemia among study participants.*

Lifestyle habits	Total (n=159)	Hyperuricemia (n=79)	Normouricemia (n=80)	X^2-value.	P-value
Alcohol intake status					
Non-drinkers	79 (49.7)	20 (25.3)	59 (73.8)		
Current drinkers	40 (25.2)	33 (41.8)	7 (8.8)	39.75	<0.0001**
Ex-drinkers	40 (25.3)	26 (32.9)	14 (17.5)		
Dietary habits					
Good	101 (63.5)	39 (49.4)	62 (77.5)	12.39	<0.0001**
Poor	58 (36.5)	40 (50.6)	18 (22.5)		
Coffee consumptions					

Lifestyle habits	Total (n=159)	Hyperuricemia (n=79)	Normouricemia (n=80)	X^2-value.	P-value
Non-drinkers	91 (57.2)	53 (67.1)	38 (47.5)		
Current drinkers	27 (17.0)	7 (8.9)	20 (25.0)	8.95	0.011*
Ex-drinkers	41 (25.8)	19 (24.1)	22 (27.5)		
Physical activity status					
Active	64 (40.3)	25 (31.6)	39 (48.8)	0.042*	4.15
Inactive	95 (59.7)	54 (68.4)	41 (51.2)		
Hydration status (USG)					
Euhydration	31 (18.3)	39 (49.4)	59 (73.8)	8.99	0.003*
Dehydration	98 (58.0)	40 (50.6)	21 (26.2)		
Cigarette smoking					
Current smokers	23 (14.5)	12 (15.2)	11 (13.8)		
Ex-smokers	34 (21.8)	18 (22.8)	16 (20.0)	0.312	0.856
Non-smokers	102 (64.2)	49 (62.0)	53 (66.2)		
Night clubbing					
Yes	45 (32.4)	31 (52.5)	14 (17.5)	25.30	<0.001**
No	114 (67.6)	28 (47.5)	86 (82.5)		
Sea food consumption					
Yes	83 (52.2)	46 (58.2)	37 (46.2)		
No	76 (47.8)	33 (41.8)	43 (53.8)	1.88	0.176
Soft drink consumption					
Yes	67 (42.1)	56 (70.9)	11 (13.8)		
No	92 (57.9)	23 (29.1)	69 (86.2)	50.90	<0.0001**
Dairy intake					
Yes	83 (52.2)	15 (19.0)	44 (55.0)		
No	76 (47.8)	64 (81.0)	36 (45.0)	20.57	<0.0001**

*significant at 5% ($p < 0.05$), **significant at 1% ($p < 0.01$)

Table 3. *Association between hyperuricemia and cardio-metabolic status of the participants.*

Clinical variables	Total (n=159)	Hyper-uricemia (n=79)	Normo-uricemia (n=80)	X^2-value.	P-value
Blood pressure (mmHg)					
Hypertensive	57 (35.8)	41 (51.9)	16 (20.0)	16.23	<0.001**
Normotensive	102 (64.2)	38 (48.1)	64 (80.0)		
Fasting Blood sugar (mg/dL)					
Diabetic	63 (39.6)	54 (68.4)	09 (11.2)	51.82	<0.0001**
Non-diabetic	96 (60.4)	25 (31.6)	71 (88.8)		
Body Mass Index (kg/m^2)					
Normal weight	74 (46.5)	18 (22.8)	56 (70.0)		
Overweight	42 (26.5)	32 (40.5)	10 (12.5)	36.27	<0.0001**
Obesity	43 (27.0)	29 (36.7)	14 (17.5)		
Waist circumference (cm)					
Normal	86 (54.1)	28 (35.4)	58 (72.5)	20.51	<0.0001**
Abnormal	73 (45.9)	51 (64.6)	22 (27.5)		
Insulin resistance					
HOMA-IR					
Normal	90 (56.6)	28 (35.4)	62 (77.5)	26.94	<0.001**
Resistant	69 (75.8)	51 (64.6)	18 (22.5)		
Urinary SG (g/ml)					
Normal	121 (76.1)	52 (65.8)	69 (86.2)	8.03	0.005
Abnormal	38 (23.9)	27 (34.2)	11 (13.8)		
Musculoskeletal disorder (MSDs)					
Yes	58 (36.5)	45 (57.0)	13 (16.2)	26.70	<0.0001**
No	101 (63.5)	34 (43.0)	67 (83.8)		
Serum Creatinine concentration (mmol/L)					
Normal	67 (79.5)	61 (77.2)	06 (37.5)	8.28	0.004
Abnormal	28 (29.5)	18 (22.8)	10 (62.5)		

The abnormal values of individual components of syndrome X were defined as: (1) BP SBP/DBP > 140/90mmHg, (2) FBS ≥ 120mg/dL, (3) BMI > 24.9kg/m^2, (4) WC > 94Cm, > 80cm for men and women respectively, (5) HOMA-IR ≥ 1.8 insulin resistance, (6) USG > 1.020g/ml dehydration, (7) hyperuricemia= >6mg/dL for women and>7mg/dL for men

Table 4. *Association between hyperuricemia and lipid sub-fractions of the participants.*

Lipid sub-fractions	Total (n=159)	Hyperuricemia (n=79)	Normouricemia (n=80)	X^2-value.	P-value
HDL (mg/dL)					
Abnormal (High)	38 (23.9)	18 (22.8)	20 (25.0)		
Normal	28 (17.6)	20 (25.3)	52 (65.0)	36.55	<0.0001**
Low	93 (58.51)	41 (51.9)	08 (10.0)		
LDL (mg/dL)					
Abnormal (High)	31 (19.5)	23 (29.1)	08 (10.0)	8.07	0.004
Normal	128 (80.5)	56 (70.9)	72 (90.0)		
TG (mg/dL)					8
Abnormal (High)	111 (69.8)	42 (53.2)	69 (86.2)	19.11	<0.0001**
Normal	48 (30.2)	37 (46.8)	11 (13.8)		
VLDL (mg/dL)					
Abnormal (High)	26 (16.4)	21 (26.6)	05 (6.2)	10.57	<0.0001**
Normal	133 (83.6)	58 (73.4)	75 (93.8)		
T-chol (mg/dL)					
Abnormal (High)	62 (80.5)	55 (69.6)	07 (8.8)	59.38	<0.0001**
Normal	97 (19.5)	24 (30.4)	73 (91.2)		

HDL = High density lipoprotein, LDL = Low density lipoprotein, TG = Triglyceride, VDDL = very low density lipoprotein, T-chol = Total cholesterol. The abnormal values for lipid sub-fractions were defined as: (1) HDL < 40mg/dL, (2) LDL >100mg/dL (3) TG >150mg/dL (4) T-chol >200mg/dL

Table 5. *Distribution of musculoskeletal pains according to body parts of participants with hyperuricemia.*

Body parts	Number of respondents	Percentages
Upper limb		
Hands/fingers	48	48.1
For arm	18	22.8
Elbow	16	20.3
Shoulder	07	8.9
Pelvic region		
Waist pain	2	3.8
Lower limb		
Hips	7	8.9
Thighs	8	10.1
Legs	6	7.6
Foots	4	5.1
Toes	5	6.3

Table 6. *Multiple logistic regression showing association between lifestyle characteristics and hyperuricemia (Odd ratios and 95% confidence interval).*

Variables	Odd ratio	95% confidence interval	p-value
Alcohol consumption			
Non-drinkers (reference)	1.00		
Current drinkers	5.199	4.249-69.623	<0.001**
Ex- drinkers	3.58	1.622-7.882	0.002**
Dietary habits			
Good (reference)	1.00		
Poor	1.23	0.982-7.2356	0.072
Coffee consumption habits			
Non-drinkers (reference)	1.00		
Current drinkers	1.320	0.543-3.212	0.540
Ex-drinkers	1.054	0.977-3.742	0.052
Physical activity status			
Active (reference)	1.00		
Inactive	2.760	0.294-25.881	0.374
Hydration status			
Euhydration (reference)	1.00		
Dehydration	2.35	1.790-9.008	0.003**
Cigarette smoking habits			
Non-smokers (reference)	1.00		
Current smokers	0.656	0.2103-2.161	0.581
Ex-smokers	1.180	0.477-2.919	0.720
Sea food consumption habits			
No (reference)	1.00		
Yes	1.217	0.559-2.648	0.621
Soft drink intake			
No (reference)	1.00		

Variables	Odd ratio	95% confidence interval	p-value
Yes	3.42	2.01-10.29	0.002**
Dairy consumption habits			
Yes (reference)	1.00		
No	1.017	0.447-2.314	0.967**
Night clubbing habits			
No	1.00	3.22-12982	0.001**
Yes	3.09		

Table 7. *Multiple logistic regression showing association between socio-demographic characteristics and hyperuricemia.*

Variables	Odd ratios	95% Confidence interval	P-value
Gender			
Male	1.000		
Female	0.906	0.498-1.647	0.746
Age (yrs)			
≤ 35	1.00		
>35	0.894	0.574-1.392	0.619
Marital status			
Single	1.00		
Married	2.24	1.947-5.303	0.006
Divorces/separate	1.12	0.517-2.419	0.776
Widowed	1.08	0.963-1.214	0.184
Monthly income (Naira)			
<10,000	1.00		
10,000-20,000	1.07	0.948-1.196	0.291
21,000-30,000	0.77	0.340-1.743	0.530
>30,000	0.52	0.241-1.115	0.093
Educational level			
Primary	1.00		
Secondary	0.72	0.271-1.910	0.509
Tertiary	0.414	0.113-1.521	0.184
Occupation			
Employed	1.00		
Unemployed	0.46	0.207-1.033	0.060
Retired	1.09	0.954-1.250	0.203
Poultry trader	0.45	0.118-1.723	0.244

Table 8. *Multiple logistic regression showing association between hyperuricemia and clinical and biochemical characteristics.*

Variables	OR	95% C.I	P-Value
Blood pressure (mm-Hg)			
Normotensive	1.00		
Hypertensive	1.60	1.280-2.008	<0.0001**
Blood sugar (mg/dL)			
Non-diabetic	1.00		
Diabetic	1.27	1.089-1.474	0.002**
Body Mass Index (kg/m^2)			
Normal weight	1.00		
Overweight	1.27	1.094-1.485	0.002**
Obesity			
Waist circumference (Cm)			
Normal	1.00		
Abnormal (High)	1.52	0.874-2.656	0.138
Insulin resistance			
Normal	1.00		
Abnormal	0.821	0.409-1.650	0.580
USG (g/ml)			
Normal	1.00		
Abnormal	1.46	0.845-2.535	0.175
Musculoskeletal disorders			
No	1.00		
Yes	3.26	1.633-6.492	0.001**
Serum Cr level (mg/dL)			
Normal	1.00		
Abnormal	0.728	0.368-1.439	0.361
HDL-C (mg/dL)			
Normal	1.00		

Variables	OR	95% C.I	P-Value
High	1.25	1.056-1.468	0.009**
Low	2.79	1.141-6.835	0.025*
TG-C (mg/dL)			
Normal	1.00		
High	4.639	3.160-21.936	0.0001**
VLDL –C (mg/dL)			
Normal	1.00		
High	1.60	1.280-2.008	0.0001**
T-chol (mg/dL)			
Normal	1.00		
High	2.33	1.149-2.535	0.0001**

BMI = Body mass index, HDL-C = High density lipoprotein cholesterol, TG-C = Triglyceride cholesterol, VLDL-C = Very low density lipoprotine cholesterol, T-chol = Total cholesterol.
*significant at 5% (P<0.05), **significant at 1% (P<0.01)

3. Statistical Analysis

The socio-demographic characteristics of study participants were analyzed using frequencies and percentages, while univariate association between the variables and hyperuricemia was examined using chi-square test. Also, the multivariate analysis was performed using multiple logistic regression models (with and without adjustment for other covariates) to identify the significant risk factors for hyperuricemia and hence odds ratios (ORs) and the corresponding confidence intervals (CIs) were estimated. P<0.05 was considered statistically significant. Data analysis was carried out using the Statistical Package for Social Sciences (SPSS version 22.0)

4. Results

The results of the present study showed that of the 159 subjects recruited for the study, 79 (49.7%) were hyperuricemic. Results of univariate association showed marital status (P=0.007) as the only demographic variable found to be significantly associated with hyperuricemia (Table 1). Also, lifestyle factors such as alcohol consumption (P<0.001), dietary habits (P<0.001), coffee consumption (P=0.011), physical activity (P=0.028), water intake (P=0.002), night clubbing (P<0.001), soft/sweet drink intake (P<0.001), yogurt intake (P<0.001) and milk consumption were significantly associated with hyperuricemia (P<0.05) (Table 2).

Tables 3 and 4 show a significant relationship between hyperuricemia and markers of cardio-metabolic disorders including BP, FBS, BMI, WC, IR, USG, MSDs, SCrand lipid sub-fractions.

Results also identified the hand/finger as the major body part affected (48.1%) while the least affected was the waist (3.8%) (Table 5).

Results of multiple logistic regression identified significant risk factors of hyperuricemia to include alcohol consumption, poor dietary habits, inadequate water intake (dehydration), and soft/sweet drink consumption (P<0.05) (Table 6).

There was increased odds for hyperuricemia among current smokers (OR=5.199, C.I=4.249-69.623), ex-smokers (OR=3.58, C.I=1.6227-7882) inadequate water consumers (OR=2.35, C.I=1.790-9.008), and soft/sweet drink consumers (OR=3.42, C.I=2.01-10.29) (Table 6).

Among all the socio-demographic variables, only marital status was found to be significantly associated with hyperuricemia with higher odds among married (OR=2.24, C.I=1.947-5.303, P=0.006) than the single, divorced or widows (Table 7).

Table 8 shows that the odds for hyperuricemia were higher in participants with abnormal cardio-metabolic status including those with hypertension (OR = 1.60, C.I=1.280-2.008, P=0.0001), type 2 diabetes mellitus (OR=1.27, C.I=1.089-1.474, P=0.002), higher than normal BMI (OR=1.27, C.I=1.094-1.485, P=0.002), abnormal WC (OR=1.52, C.I=0.874-2.656, P=0.138), higher than normal USG (OR=1.46, C.I=0.845-2.535, P=0.175) and MSDs (OR=3.26, C.I=1.633-6.492, P=0.001).

Also, dyslipidemia was associated with higher odds for hyperuricemia, with hypertriglyceridemia conferring the highest odds (OR=4.639, C.I=3.160-21.936, P=0.0001) for hyperuricemia on participants.

5. Discussion

The results of this cross-sectional study showed that some demographic factors, over-indulgence in some unhealthy behaviors, abnormal anthropometric indices, and the presence of some metabolic aberrations drive the high prevalence of hyperuricemia among study participants as observed in the general population [15].

The postulated pathophysiological mechanisms underlying these observations are related in part, to the interference with synthesis, metabolism or excretion of UA or a combination of the above mentioned by several lifestyle habits or metabolic disorders. For instance, the evidence that explains the association between alcohol intake and increase SUA level is based on two pathophysiological processes. First, the metabolism of alcohol involves the conversion of acetate to acetyl coenzyme A with a resultant increase in the breakdown of adenosine triphosphate (ATP) to adenosine monophosphate (AMP), and leading to increase UA synthesis [13]. Second, alcohol intake/metabolism induces lactic acidemia. Lactic acidemic state is known to cause hyperuricemia by two processes; first, by decreasing UA

excretion through the urine [16-19] second, by increasing UA re-absorption by the renal tubules [20] and leading to hyperuricemia.

Compared to other life style related risk factors for hyperuricemia, alcohol intake was associated with the highest odds for hyperuricemia in the present study which is in accordance with a growing number of studies demonstrating positive correlation between habitual alcohol intake and incident hyperuricemia [16, 21].

According to Sun et al [22], chronic alcohol consumption remains the most consistent risk factor for hyperuricemia even when other previously implicated dietary components failed to attain level of statistical significant association with hyperuricemia [23].

Inadequate hydration status was significantly associated with increased odds for hyperuricemia, with dehydrated participants having greater than 2 times more likelihood of being hyperuricemic. This can be explained by the fact that prolonged dehydration causes hypovolemia, poor renal plasma flow with a resultant renal hypoperfusion episodes, decreased glomerular filtration rate (GFR), increased sympathetic nervous system discharge, reduction in renal urate clearance and leading to hyperuricemia [24, 25]. The found association between physical inactivity and increased odds for hyperuricemia among participants is likely due to the effects of its association with important risk factors of hyperuricemia including poor hydration status [26], obesity and other metabolic disorders. This finding is consistent with earlier reports that showed inverse association between physical activity status, smoking habits, SUA level and associated mortality [27]. However, a number of human studies have reported higher SUA on prolonged exercise, suggesting the heterogeneous responses of SUA level to the effect of exercise. Again, this can be explained by the fact that prolonged physical activity increases the odds for dehydration.

The frequency of hyperuricemia was also higher in male than female participants probably because of the uricosuric effect of estrogen in females [28], and the fact that men have SUA levels that are closer to the urate saturation threshold (6.8mg/dl) [29, 30]. Hence, even a slight increase in SUA level may be quantitatively relevant for the diagnosis of hyperuricemia in men.

Marital status showed significant association with hyperuricemia. Hyperuricemia was more frequent among married subjects, and retained significance in the multivariate analysis. Being married was associated with greater than 2 times odds of being hyperuricemic than others. There are several plausible explanations for this association. First, changes in marital status have been found to also influence dietary habits and lifestyle choices either positively or negatively including composition and quality of diets as well as physical activity status. Mounting evidence shows that marriage could influence body weight through dietary quality and quantity and leading to the attainment of high body weight.

There is also clear evidence suggesting higher risk of overweight and obesity among married people [31, 32] than the unmarried ones. Obviously, overweight and obesity are associated with several other metabolic aberrations known to cause hyperuricemia including T2DM, hypertension, dyslipidemia, IR, renal function impairment and deranged UA metabolism.

The finding of a significant association between marital status and higher risk of hyperuricemia in the present study agrees with this line of reasoning given that married participants constituted the highest proportion of the present study population. Furthermore, a recent study found that being married could also increase the risk of dehydration (a known risk factor for hyperuricemia) especially married individuals of lowest educational levels, with no spouse present, and in particular those in lower socio-economic classes and temporarily employed workers [26]. The above demographic characteristics are consistent with those of the present study population.

Night clubbing habits increased the frequency and risk of hyperuricemia among participants probably due to poor dietary and life-style related habits that are common among night clubbers. At night clubs and drinking joints/bars, clubbers engage in binge drinking of alcoholic beverages, expose to first and second hand tobacco smoking/indoor air pollutants, eat junk foods/meats dense with high cholesterol and low in fruits/vegetables, and other risk factors that predispose them to abnormal uric acid metabolism and excretion and leading to hyperuricemia [33].

Furthermore, participants with metabolic syndrome (MS) clusters (obesity, hypertension, T2DM, dyslipidemia and IR) as well as MSDs had higher frequency and odds for hyperuricemia than those without these disorders. This finding is in line with several epidemiologic studies from different populations. For instance, in a cross-sectional study conducted by Cardoso et al [34] in Camino Grande, a state of Paraiba, Brazil on the association between SUA concentration according to the presence of non-alcoholic fatty liver disease and metabolic syndrome in overweight or obese children and adolescents, the authors found out that the participants with MS clusters had higher odds for hyperuricemia than those without these disorders. In USA, a positive correlation has been observed between increase incidence of MS cluters and a progressive increase in SUA levels over the past 100 years [35]. Also, in a one year case-control study conducted in Bikaner, Rajasthan, India, Khichar et al [36] reported significant association and positive correlation of mean SUA level with all components of MS except serum HDL-C. Similarly, a population of Pima Indians in Gila River Indian community is reported to have experienced high prevalence of hyperuricemia among obese and T2DM patients. This followed a transition from traditional to modern lifestyle, most especially changes in food supply and dietary habits [37-41], similar to the observation in the present study, where poor dietary and life style habits (low fruits and vegetable consumption, poor hydration status, alcohol consumption, night clubbing, cigarette smoking etc.,) were associated with higher odds for

hyperuricemia among participants.

However, several other studies have demonstrated a non-linear relationship between plasma glucose and SUA level. Wang et al [42] reported a U-shaped relationship between fasting plasma glucose and SUA. Other investigators [43-46] document a curvilinear correlation between plasma glucose and SUA level, both in the general and diabetic populations.

Participants with high SUA level had increased odds for T2DM probably because of the inhibitory effect of hyperuricemia on β-cell function and hence insulin secretion as demonstrated by other investigators [47]. This also explains the higher prevalence of IR among participants with hyperuricemia in the present study. This observation supports the notion that IR is one of the fundamental mechanisms behind hyperuricemia [48, 43]. Also, it is interesting to note that although hyperuricemia increased the odds for T2DM, not all hyperuricemic participants were diabetic. This observation supports the hypothesis that hyperuricemia might have a protective effect/action against β-cell dysfunction and IR as well as the notion of individual differences in effect of hyperuricemia on beta-cell function.

Many studies [44, 49] have shown that hyperuricemic state can improve β-cell function, augments insulin secretion and improve glycemic control, glycosylated hemoglobin (HbAIc) and by extension protects against onset of T2DM. These effects are attributable to the antioxidative action of UA which protects against apoptosis, improve β-cell function and enhance insulin secretion [46, 50]. Correlation study by Gill et al [51] reported linear increase in SUA level and serum insulin level. Conversely, it is noteworthy that not all diabetics in the present study were hyperuricemic. This finding supports the speculation that diabetes mellitus state may reduce future risk of hyperuricemia/gout due to the uricosuric effect of glucose [52].

The risk of hyperuricemia was higher among obese participants (higher BMI and WC). This has also been found in a previous study showing a strong correlation between SUA level and abdominal obesity [53], likely due to the effect of hyperuricemia on serum leptin level. Collaborative studies by Fruehwald-shultes et al [54] and Bedir et al [55] independently found positive correlation between SUA and serum leptin concentration, suggesting a plausible mechanistic link between hyperuricemia and obesity. Adiposity-induced IR is also thought to cause hyperuricemia, probably by impairing UA clearance by the kidney [53]. In agreement with this line of reasoning, de Oliveira and Burini [56] reported a lower UA clearance in obese than non-obese subjects, also suggesting decrease renal clearance of UA as a plausible mechanism of hyperuricemia in obesity.

The increased odds and prevalence of hypertension observed among participants with hyperuricemia in the present study has been reported previously [57-59], and is ascribable to various metabolic and vascular aberrations associated with hyperuricemia including high SUA level-induced depletion of nitric oxide and leading to vasoconstriction [60], increased salt retention [61], increased serum triglyceride levels and chronic inflammation [62]. There is also associated nephrosclerosis (glomerular sclerosis, arteriosclerosis and interstitial fibrosis) leading to increase renal vascular resistance, impaired glomerular filtration rate (GFR) and poor urate clearance [57]. Hyperuricemia-induced IR is also associated with several vascular abnormalities including vasospasm, increased vascular reactivity and intracellular calcium concentration, formation of proinflammatory agents, platelets aggregation and endothelial dysfunction. A prospective study by Sundstrom et al [59] showed that hyperuricemia precedes onset of hypertension.

A greater number of the participants with high SCr also had hyperuricemia, suggesting a decrease in renal clearance of Cr which could have also affected UA clearance and causing hyperuricemia. The poor clearance of UA by the kidney accounts for greater than 90% cases of hyperuricemia [63]. In fact, it is posited that the kidney plays a more significant role in maintaining normal SUA level than dietary factors [22].

Poor dietary habits increased the odds for hyperuricemia among participants in the present study. This observation supports results of numerous trials and meta-analysis showing that SUA levels can be lowered to near normal range with restriction or moderation in diets particularly the high purine and fat diets. For instance, the consumption of sugary foods, red meats, sea-foods, high fructose containing diets and sugar sweetened beverages have been implicated in the pathogenesis of hyperuricemia. Conversely, increase intake of low-fat dairy products, whole grains, coffee, nuts vegetables and legumes has been shown to decrease the risk of hyperuricemia and therefore are frequently recommended in the management of hyperuricemia and gout.

6. Conclusion

The increasing prevalence of undiagnosed hyperuricemia among patients seeking care from primary care physicians and in the general population underscores the urgent need for improvement in the effort to identify and manage risk factors of hyperuricemia as an important step for early prevention of the disease and associated complications.

Several limitations of the present study should be considered in the interpretation of the results of this study, especially those related to the cross-sectional nature of the study design. For instance, one cannot claim causality because of the cross-sectional nature of the study. Also, this one-point measurement represents a temporary but not a permanent effect. Furthermore, self reported personal characteristics and lifestyle habits are prone to over and under estimation.

Acknowledgements

We are thankful to the management of the health facility where the work was carried out. We are also grateful to Mr. Sampson Kayode for his numerous contributions to the success of this work.

Competing Interest

None declared.

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