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Research Article

Assessing Serum Uric Acid Levels in Heart Failure: A Multicentred Study in Cameroon

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Abstract

Background: Heart Failure is responsible for about 26 million patients annually, with an increasing burden occurring in low- and middle-income countries. High serum uric acid levels have been consistently reported in the prognosis of heart failure. The exact mechanism to an increase production of uric acid in heart failure is however unclear. Assessing serum uric acid may allow rapid and cost-effective determination of clinical prognosis of patients with heart failure. Very few studies have been conducted to assess serum uric acid levels in patients with heart in Africa and Cameroon, where heart failure incidence, prevalence, morbidity and mortality are on the increase.

Objective: To determine serum uric acid levels in patients with heart failure and assess the relation between serum uric acid levels and the severity of heart failure.

Methods: Our study was a multicentre cross-sectional study in which 200 heart failure patients were included. Patients presenting hyperuricemia, gout or on urate lowering drugs were excluded. New York heart association (NYHA) functional classification and left ventricular ejection fraction classification was used to assess severity. Hyperuricemia was defined as serum uric acid levels > 6mg/dl in both males and females.

Results: The mean age of our population was 64.81 +/- 14.61years, in which females were 54%. Overall, 56.6% (162/187) met the definition of hyperuricemia with a mean value of 8.56 +/- 3.20 mg/dl. Hyperuricemia was associated with clinical course (P 0.031), and the prevalence of hyperuricemia was 100% in patients with acute heart failure, 95% in patients with chronic decompensated heart failure and 81.54% in patients with chronic stable patients. Patients with NYHA III/IV accounted to 54.6% of hyperuricemic patients, and 33.3% of hyperuricemic patients had a reduced ejection fraction. Serum uric acid levels increased with increasing NYHA class and reducing left ventricular ejection fraction. There was a significant association between serum uric acid levels, NYHA (OR 0.39 95%CI 0.16-0.96 P value 0.0035) and reduced ejection fraction (P value 0.002).

Conclusion: more than half of patients with heart failure have hyperuricemia. High values of serum uric acid are associated to severe heart failure. Serum uric acid could provide additional prognostic information in heart failure. Serum uric acid level can be measurement anywhere at low cost and would help identify high-risk patients. Lowering Uric acid in patients with heart failure may be the new approach for treating patients with heart failure.

Keywords: Heart Failure; Serum Uric Acid; Severity; Clinical Prognosis

Introduction

Heart Failure (HF) is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood [1]. Its diagnosis is based on clinical presentation, radiographic and laboratory investigations [1]. HF affects an estimate of 26 million patients annually worldwide [2,3]. This

global incidence rate appears to remain stable over the years and this might be bound to increase as population gets older [4]. In the United States (US), the prevalence of HF is about 3.9% with an incidence of more than 550000 persons each year [5]. Whereas in Europe, the prevalence of HF is lower and is maintain around 1-2% among adults, and its incidence has been on the steady increase from 895 in 100000 persons per year in 2000 to 2126 cases in 2007 [1]. Unlike in the developed world, there are no population-based incidence and prevalence studies of HF from Africa where it is a major burden [6, 7]. HF accounts for 1-2% of the estimated health budget in developing countries; similar to the economic impact of HF in developed countries as youths are the mostly affected [8-10]. More admissions of HF are being recorded worldwide including In SSA with close to 3-7% of Cardiovascular disease (CVD) admissions [14,15]. In Cameroon, Boombhi., *et al*. in 2017 estimated that HF accounts for 33.3% of CVD admissions [16,17]. In the general population, HF carries a poor prognosis especially in the presence of concomitant diseases and confers a fivefold increase in the risk of sudden death [18]. It is a major challenge to objectively channel clinical decisions early, thus markers of severity are of need [19]. This is dependent on clinical predictors such as New York Heart Association (NYHA) class, echocardiographic parameters such as left ventricular ejection fraction, electrocardiogram parameters (QRS prolongation and presence of atrial fibrillation), neurohumoral activation, heart rate variability, blood pressure, weight, presence of an S3 gallop or jugular venous pressure and cardiothoracic ratio [20,21]. A number of biomarkers of severity of HF exist; brain natriuretic peptides, NT-Pro BNP, atrial natriuretic peptides, blood urea nitrogen, cardiac troponins, cystatin C, red cell distribution width, blood glucose level, creatinine, C-reactive protein, serum cholesterol level, albuminuria, haemoglobin level, cytokines level, endothelin level, and serum uric acid (UA) level [21,22]. An ever growing interest in UA has emerged, because of its wide availability and low cost. Hyperuricemia (HU) has been shown to be a constant feature of metabolic imbalance within HF pathophysiology and has been identified as an independent severity marker comparable and even stronger than previously established biomarkers [23]. In developed countries, hyperuricemia (HU) has been revealed to be an independent marker of poor prognosis in patients with chronic HF [24-26]. In developing countries, the prevalence of HU is high and has a potential link with cardiovascular complications [27]. In SSA, Longo., *et al.* established a positive relationship between HU and risk for CVD in Kinshasa-Congo [28], Black Africans with myocardial infarction and HU, had markedly reduced left ventricular ejection fraction and increased mortality [29]. But, no study from the best of our knowledge has been done in Cameroon on assessing serum UA levels in HF patients; beside serum UA is a useful and affordable cost effective severity marker in HF [23,24]. The use of serum UA levels as a prognostic factor in HF has been assessed and validated in many western countries but few studies has been done in an African milieu. Hence the objective of this study is to assess serum uric acid levels in patients with heart failure. Specifically to describe the socio-demographic and clinical profile of patients with heart failure; to determine serum uric acid levels of patients with Heart failure and to correlate serum uric acid level and severity of heart failure.

Materials and Methods

Study Design

This study was a hospital based cross-sectional study.

Period of Study

From 15th January to 30th March 2018, a total of two and a half months.

Site of study

This study was a multicentre study in the cities of Yaounde and Douala. Participants were recruited at the Cardiology Units of: The Douala General Hospital, Laquintinie Hospital Douala and Yaounde Central Hospital.

Douala is the economic capital of Cameroon and is the headquarters of the Littoral region with a population of about 3 million people and is situated in the Gulf of Guinea.

The Douala General Hospital is a tertiary university teaching hospital whereas The Laquintinie hospital Douala is a second category teaching hospital. They all have a cardiology unit with 4 main sectors; outpatient's consultation, hospitalization sector, cardiology intensive unit and a cardiology exploratory room. Yaounde is the political capital of Cameroon and, with a population of approximately 2.5 million, the second largest city in the country after the port city Douala. The central hospital Yaounde, is a second category university teaching hospital.

Study population and sampling

Target population

Our target population was made up of patients with HF seen at the cardiology units of the above centres on out-patient and hospital admission base.

Inclusion Criteria

All patients diagnosed of heart failure consenting to be part of the study. HF was diagnosed according to the Framingham criteria (table iii).

Exclusion Criteria

- Patients with secondary hyperuricemia: Malignancies and drug-induced such as pyrazinamide, ethambutol, cyclosporine, diclofenac (except diuretics and salicylates)
- Patients with a documented past history of gout or on urate lowering therapy.
- Patients with end-stage renal failure or patients on haemodialysis.

$$n_o = \frac{Z^2pq}{2}$$

Sample Size determination

The minimum sample size is estimated using the formula of Cochran:

Where No = sample size

Z: selected alpha level is 1.96 at 95% confidence interval

p: was the prevalence of hyperuricemia in patients with heart failure. But in the absence of this data in CMR, by convenience the Prevalence of hyperuricemia in patients with Heart failure in Italy which was 60% was used.

Q: 1-p= 0, 557

e: level of precision, at 5% e=0,05.

No= 369 participants.

So, the minimum sample size required was 369 participants.

Sampling was consecutive and non-exhaustive.

Ethical consideration

Ethical clearance was gotten from the institutional review board (IRB) of the University of Buea. The Authorization to do research was gotten from the dean of the Faculty of Health Sciences, University of Buea. Administrative approval and authorization were gotten from the Director of the Douala General Hospital. Administrative approval and authorization were gotten from the Director of the Laquintinie hospital Douala.

Study Procedure

After ethical approval was gotten, data collection from participants was done. This was done through an investigator supervised interview, clinical examination and collection of information from the medical records of participants.

Invitation and Selection of Participants

Potential study participants were approached in the cardiology units by the primary investigator once a diagnosis of Heart failure was made. The potential participants were then assessed by questions and medical record checking for any past history of hyperuricemia or use of urate lowering drugs. If this was found, the participant was excluded from the study and thanked for their time. Participants eligible were then included and a questionnaire was filled by the primary investigator.

Sociodemographic parameters

During the interview the following parameters were gotten by asking direct and clear questions in the language best understood by the participant: Age in years; Sex; Profession; Level of education; Ethnicity; Address; Marital status

Clinical parameters

This parameter was assessed either through direct and closed questions or through a physical examination.

- **Direct questions:** Participants were questioned about; Past diagnosis of heart failure, duration since diagnosis, treatment taken for HF.; Complications since diagnosis of HF such as; Arrhythmia, cerebrovascular accident, transient ischemic stroke, deep venous thrombosis, acute kidney injury and chronic kidney disease; Comorbidities associated to HF such as; Human immunodeficiency virus/ Acquired immunodeficiency syndrome, chronic obstructive pulmonary disease, malignancies, blood disorders and chronic non-inflammatory diseases; Past diagnosis and treatment for hypertension, diabetes and dyslipidaemia; Physical activity routine; Smoking and alcohol abuse. Symptoms of HF they presented when seen such as; dyspnoea, nocturnal cough, orthopnoea, paroxysmal nocturnal dyspnoea, chest pain and palpitations.
- **Physical examination:** Weight. Height. Abdominal circumference. Body Mass Index (BMI) was calculated using the formula; weight/height in metres2. Blood pressure. Heart rate. Respiratory rate. Neck vein distention. Hepatojugular reflux. Bilateral ankle oedema. Heart auscultation. Lung Auscultation. Mild to moderate HF: was defined as either NYHA class 1 to 2, or a preserved or mid-range EF class. Severe HF: was defined as either NYHA class 3 to 4, or a reduced EF class. a- New York heart association classification this classification was done as such [32]; Left ventricular ejection fraction Participants left ventricular ejection was assessed on echocardiography. Data Collected from the Patient Record. Echographic details such as; EF and HF aetiology. Serum creatinine value from which creatinine clearance was calculated using the CKD-EPI formula.

Biological parameters

Sample collection

Blood was collected after clinical assessment for analysis. Collection was done on day one of admission from the participants admitted into the ward (with acute heart failure and chronic decompensated heart failure) after an overnight fasting, and on any day from those met at outpatient department if they are in a fasting state or an appointment for sample collection was made with the participants agreement. The collection tube was labelled with the participant's serial number after sample collection.

Sample Transport and Storage

After sample collection, the tube was immediately labeled with the participant's serial research number placed in an ice-packed cooler and transported to the laboratory for analysis. The blood samples collected at the end of the day were centrifuged using a Hettich universal 320/320r centrifuge machine. Centrifugation was done during five minutes at a speed of 2500 to 3000 rotations per minutes. 500 µl of Serum from each tube was collected using a pipette and transferred into Eppendorf microcentrifuge tubes. The receiving Eppendorf microcentrifuge tube had the correct and corresponding serial number of the participant. The micro tubes were then stocked into a fridge at -20°C until day of analysis. UA level was measured using the enzymatic-colorimetric method. This was done using the fully automated COBAS C311 Hitachi Roche test at the biochemistry laboratory of the Douala General Hospital.

Results and Discussion

Participants enrolled into the study

A total of 250 heart failure patients were met during our stud.50 were excluded: 45 had reported hyperuricemia before the diagnosis of heart failure was made, 5 had gout and were treated with urate lowering drugs. So, 200 participants were eligible and were all included in the study.

Sociodemographic profile of our study population

A hundred-and-eight (54%) were females while 92 (42%) were males. The male to female ratio was 1:1.17. The median (25th - 75th) age of participants was 68 (54-76) years, with extremes of 21 to 96 years. In the population, 54.6% of females and 55.4% of males had ages ranging between 61 and 80 years.

Clinical profile of study population

Clinical presentation

A hundred and thirty-four participants (67%) had dyspnoea, 62 (31%) had nocturnal cough and 54 (27.5%) had orthopnoea. A participant could present with more than one symptom. The mean population BMI was 27.76 +/- 8.19 kg/m2 with extremes of 16.9 to 83.2 kg/m2. Clinically, 52 (26.80%) participants were overweight and 58(30%) were obese. The mean abdominal circumference was 93.14+/- 18.95. The mean abdominal circumference was 93.4 +/- 16.2 kg/m2 and 92.8 +/- 21.0 in females. On examination, the mean pulse was 86.91 +/- 49.95 beats per minutes. Forty-three (21.5%) participants had an arrhythmia; The mean systolic blood pressure was 133.90+/- 30.06 mm hg and the mean diastolic blood pressure was 85.05 +/- 20.12. on auscultation, 39 (19.5%) had a murmur and 52 (26%) had crackles. Fifty-two (26%) participants had lower limb oedema.

Clinical course

The median duration of disease was 3(1 - 6) years. Thirty-seven (18.5%) were acute HF patients, 20(10%) were chronic decompensated HF patients and a hundred and 3(71.5%) were chronic stable patients.

Traditional cardiovascular risk factors

In our population, hypertension was found in 110(55%) participants, 26 (13%) were diabetics, and 25(12.50%). Thirteen (6.50%) of our participants were smokers with a median smoking duration of 13.50(10 -26.75) months.

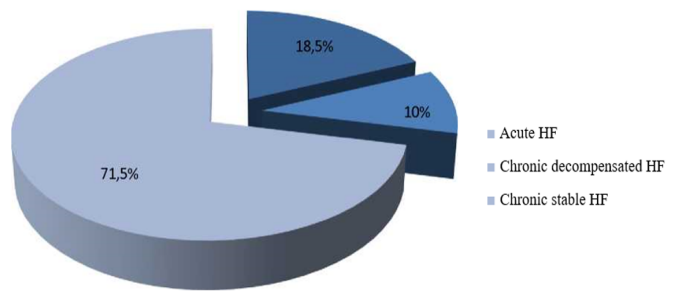

Figure 1: Clinical course distribution of our population had a history of dyslipidaemia.

The median smoking index was 2.5(0.22 - 12.70) pack years. Seventy-six (35%) of participants consumed alcohol, with a median alcoholic index of 2.00(2 - 8). A hundred and seventy-eight (89%) had a sedentary lifestyle while 19(9.5%) had a regular physical activity with a median frequency of 3 (1 - 6.25) times per week.

Cardiovascular risk factors	Males		Females		Total	
	n n	% %	n	% %	n	% %
Hypertension	51	55.40	59	55.70	110	55
Diabetes	16	17.40	10	9.40	26	13
Smoking	9	9.80	4	3.70	13	6.50
Physical inactivity	81	88	97	90.70	178	89
Alcohol	38	41.30	38	35.20	76	38
Dyslipidaemia	16	17.40	9	8.30	25	12.50
Obesity	19	20.70	39	36.10	58	30

Table I: traditional cardiovascular risk factors in the study population.

Echographic features : Left ventricular ejection fraction

The median left ventricular ejection fraction of the study population was 51 (35 - 64.80)%. Left ventricular ejection fraction ranged between 12 and 86%. Eighty-two (52.6%) had preserved EF, 28(17.9%) had mid-range EF and 46(29.5%) had reduced EF. Considering each clinical course, 20 (35.08%) of acute HF participants had preserved EF, 15(68.18%) of Chronic decompensated had reduced EF and 57(51.82%) of chronic stable HF participants had preserved EF. Forty-four participants did not have echocardiography done.

Aetiology of heart failure

A hundred-and-nine (54.5%) participants had a myocardial disease and 103 (51.5%) had a Valvular disease.

LVEF	Acute HF		Chronic Stable HF		Chronic Decompensated HF		Total	
	n	%	n	%	n	%	n	%
Preserved EF	20	54.1	57	57.0	5	26.30	82	52.60
Mid-range EF	3	8.10	23	23.0	2	10.50	28	17.90
Reduced EF	14	37.80	20	20	12	63.20	46	29.50
Total	37	100	100	100	19	100	156	100

Table 2: Left ventricular ejection fraction classification in each clinical course.

Treatment of heart failure

A hundred and forty-three (71.5%) of participants were on treatment for heart failure. The median duration of this was 36(12 - 72) months. A hundred and twenty-nine (64.80%) were on diuretics and 85(42.50%) were on angiotensin converting enzyme inhibitor. Of those on diuretics; 117(58.50%) were on thiazides, 5(2.50%) were on potassium sparing diuretics and 7(3.5%) were on loop diuretics. Some participants were on more than one drug.

Kidney involvement in heart failure patients

The mean serum creatinine was 1.15+/- 0.7mg/dl with extremes ranging from 0.1 to 3.66 mg/dl. The mean Creatinine clearance was 70.3 ml/min/1.73m^2 with extremes of 12 to 241 ml/min/1.73m^2. Thirty-five (32.4%) of participants had no kidney involvement.

GFR ml/min	Number	Percentage
CKD 1 (>90)	35	32.4
CKD 2 (<89 - >60)	35	32.4
CKD 3a (<59 - >45)	11	10.2
CKD 3b (<44 - >30)	18	16.7
CKD 4 (<29 - >15)	6	5.6
CKD 5 <15	3	2.8

Table 3: CKD classification of creatinine clearance.

Severity of heart failure

Severity assessment using NYHA classification and description of severe heart failure patients.

In our population, 24 (12%) were NYHA class 1, 76 (38%) were NYHA class 2, 65 (32.5%) were NYHA class 3, 35 (17.5%) were NYHA 4. A total of 100 (50%) of participants had mild to moderate HF, and 100 (50%) had severe HF. Of these patients with severe HF, 34 (34,34%) had acute HF, 18 (18,18%) had chronic decompensated HF and 47 (47,48) had chronic stable HF. Severe heart failure population had 54 (54,55%) females and 46 (46,47%) males. The average of these patients was 65.9+/-15.4 years. Twenty-eight (28.28%) severe HF patients had no level of education and 33 (33.33%) had secondary school education. Among severe heart failure patients: 58 (58.59%) had hypertension, 17 (17.18%) had diabetes, 11 (11.11%) had dyslipidaemia, 7 (7.07%) were smokers and 44 (44.44%) consumed alcohol. The mean systolic blood pressure of patients with severe heart failure was 135+/-33.8 mmhg

and the diastolic was 86.5+/-22.3 mmhg. Thirty-two (32.32%) of these patients had a preserved ejection fraction, and 23 (23.23%) had reduced ejection fraction. Thirty (30.30%) had myocardial heart disease. Twenty-three were CKD 2 and 3 (3.03%) were CKD 5. The mean serum uric acid level of patients with severe heart failure was 9.4+/-37 mg/dl.

Characteristics	Mild to moderate HF	Severe HF	OR	CI at 95%	P value
BMI (mean + SD)					
Underweight	3(37.5%)	5(62.5%)	0.60	0.14 - 2.58	0.721
Normal weight	93(50.0%)	93(50.0%)	1.67	0.39 - 7.18	0.721
Overweight	25(48.1%)	27(51.9%)	0.93	0.49 - 1.75	0.812
Obesity	35 (60.3%)	23 (39.7%)	1.84	0.98 - 3.45	0.057
Aetiology of HF n (%)					
Valvular disease	35(56.5%)	27(43.5%)	0.85	0.43 - 1.72	0.657
Hypertensive	29(63.0%)	17(37.0%)	1.34	0.64 - 2.81	0.433
Myocardial disease	35(53.8%)	30(43.2%)	0.68	0.34 - 1.34	0.286
Pericardial disease	1(50%)	1(50%)	0.70	0.04 - 11.5	1.000
Endocarditis	0(00%)	1(100%)			0.415
Unknown	2 (22.2%)	7 (77.8%)	0.30	0.06-1.59	0.167
Others	2(66.7%)	1(33.3%)	1.4	0.13 - 16.2	1.000
Risk factors n(%)					
HTN	52(47.3%)	58(52.7%)	0.77	0.43 - 1.37	0.378
DM	9(34.6%)	17(65.4%)	0.50	0.21 - 1.20	0.116
Dyslipidaemia	14(56.0%)	11(44.0%)	1.53	0.63 - 3.74	0.352
Smoking	6(46.2%)	7(53.8%)	0.84	0.27 - 2.59	0.783
Alcohol	44(57.9%)	32(42.1%)	1.65	0.93 - 2.94	0.089
CKD Classification (n+%)					
CKD 1	17(50%)	17(50%)	2.04	0.89 - 4.67	0.090
CKD 2	12(34.3%)	23(65.7%)	0.77	0.33 - 1.80	0.550
CKD 3a	6(54.5%)	5(45.5%)	2.09	0.60 - 7.36	0.328
CKD 3b	6(33.3%)	12(66.7%)	0.77	0.27 - 2.25	0.633
CKD 4	0(00%)	6(100%)			0.080
CKD 5	0(00%)	3(100%)			0.284
Age in years (mean + SD)	63.7± 13.8	65.9±15.4			0.282
Blood pressure					
SBP (mean + SD)	132.6±25.4	135.1±33.8			0.567
DBP (mean + SD)	83.5±17.3	86.5±22.3			0.323
Serum UA levels	7.7±2.3	9.4±3.7			<0.001

Table 4: Clinical characteristics of patients with mild-to-moderate heart and severe heart failure participants using NYHA 1.

There was a statistically significant association between severity of heart failure and the following: serum uric acid level (P value <0.001), chronic stable HF (OR 21.02 95%CI 0.02¬0.4 P value <0.001) and acute HF (OR 0.06 95%CI 0.02-0.20 P value <0.001). On multivariate analysis, only chronic stable clinical course had a significant association (adjust OR 17.31, 95%CI 3.48-86;14, P value <0.001).

Characteristics	Mild to moderate HF	Severe HF	OR	CI at 95%	P value
Gender					
Females	54 (50)	54 (50)	0.97	0.56-1.71	0.938
Males	46 (50.5)	45 (49.5)	/	/	/
Level of Education					
None	19 (40.4)	28 (59.6)	0.60	0.31-1.16	0.122
Primary school	32 (52.5)	29 (47.5)	1.14	0.62-2.07	0.679
Secondary school	39 (54.2)	33 (45.8)	1.28	0.72-2.28	0.405
University	10 (52.6)	9 (47.4)	1.11	0.43-2.86	0.827
Clinical course					
Acute HF	3 (8.1)	34 (91.9)	0.06	0.02-0.20	< 0.001
Chronic	2 (10)	18 (90)	0.09	0.02-0.40	< 0.001
decompensated HF					
Chronic stable HF	95 (66.9)	47 (33.1)	21.02	7.87-56.12	< 0.001
Left ventricular ejection fraction					
Preserved	43 (53.1)	38 (46.9)	2.21	0.68-2.13	0.507
Mid-range	17 (60.7)	11 (39.3)	1.64	0.73-3.70	0.231
Reduced	14 (30.4)	32 (69.6)	0.34	0.17-0.69	0.002

Table 5: clinical characteristics of mild-to-moderate and severe heart failure patients using NYHA 2.

Characteristics	Ajusted OR	CI at 95%	P ajusted
Serum UA levels	1.00	0.87-1.16	0.988
Acute HF	0.79	0.12-5.20	0.810
Chronic stable HF	17.31	3.48-86.14	< 0.001

Table 6: Multivariate analysis between clinical parameters and severity of heart failure using NYHA.

Severity assessment using left ventricular ejection fraction and description of severe heart failure patients

In our general population, 82 (41%) had preserved EF, 28 (14%) had mid-range EF and 46 (23%) had reduced EF. Considering each clinical course, 20 (54.10%) of acute HF patients and 57 (57%) of chronic stable patients had preserved EF, while 12 (63.2%) of chronic decompensated HF patients had reduced EF. A total of 110 (70.5%) had mild to moderate HF and 46 (29.5%) had severe HF according to severity assessment using ejection fraction in the general population. Severe heart failure patients in this classified had a mean age of 61.6+/-16.5 years. Twenty- two (47.83%) were females and 24 (52.17%) were males. Fourteen (37.8%) had acute HF patients, 20 (20%) had chronic stable HF patients and 12 (63.2%) chronic decompensated HF. Fifteen (41.30%) and 17 (36.96%) were classified NYHA III and IV respectively. Their mean systolic and diastolic blood pressures were 131.3+/-26.9 and 85.9+/-17.7 mmgh. Among those severe HF participants: 23 (50%) were hypertensive, 7 (15.22%) had diabetes, 4 (8.70%) had dyslipidaemia, 3 (6.52%) were smokers and 19 (41.30%) consumed alcohol. Sixteen (34.75%) had valvular heart disease and 23 (50%) had myocardial disease.

	General Population		Acute HF		Chronic HF			
					Stable		Decompensated	
	n	%	n	%	n	%	n	%
Mild to moderate HF	110	70.5	23	62.2	80	80	7	36.8
Severe HF	46	29.5	14	37.8	20	20	12	63.2
Total	156	100	37	100	100	100	19	100

Table 7: Heart failure classification using left ventricular ejection fraction.

There was a statistically significant association between severity of heart failure and the following: myocardial disease (OR 0.28 95%C10.11-0.74 P value 0.008),serum uric acid (P value 0.002), chronic decompensated HF (OR 1.93 95%CI 0.007-0.53 Pvalue 0.001), chronic stable HF (OR 3.46 95%CI 1.70-7.11 Pvalue 0.001), NYHA II (OR 2.46 95%CI 1.14-5.35 P value 0.018), NYHA IV (OR 0.29 95%CI 0.13-0.65 P value 0.002). After multivariate analysis, myocardial disease had a significant association (adjust OR 0.28, 95%CI 0.09-0.90, P value 0.033).

Serum uric acid levels in the study population and description of the hyperuricemic group

The prevalence of hyperuricemia in our study was 56.5%. The median was 7.55(6.40 - 9.9), serum uric acid levels ranged from 3.9

Characteristics	Mild to moderate	Severe	OR	CI at 95%	P value
	HF N (%)	HF N (%)			
BMI (mean + SD)					
Underweight	3(60)	2 (40)	0.61	0.10 - 3.93	0.637
Normal weight	104(70.3)	44 (29.7)	1.67	0.39 - 7.18	0.637
Overweight	33(75.0)	11 (25.0)	1.42	0.64 - 3.13	0.385
Obesity	33 (75**)**	11 (25)	1.29	0.58 - 2.88	0.528
Aetiology of HF n (%)					
Valvular disease	38(70.4)	16 (29.6)	1.00	0.43 - 2.37	0.986
Hypertensive disease	23(76.7)	7 (23.3)	1.57	0.59 - 4.20	0.362
Myocardial disease	34(59.6)	23 (40.4)	0.28	0.11 - 0.74	0.008
Pericardial disease	1(50)	1 (50)	0.41	0.03 - 6.85	0.508
Endocarditis	0(00)	1 (100)			0.297
Unknown	1(50)	1 (50)	0.41	0.03 - 6.85	0.508
Risk factors n (%)					
HTN	62(72.9)	23 (27.1)	1.1	0.53 - 2.28	0.792
DM	15(68.2)	7 (31.8)	0.84	0.32 - 2.24	0.732
Dyslipidaemia	16(80.0)	4 (20.0)	2.22	0.67 - 7.38	0.185
Smoking	6(66.7)	3 (33.3)	0.83	0.20 - 3.46	0.724
Alcohol	47(71.2)	19 (28.8)	1.04	0.51 - 2.09	0.919
CKD Classification (n+%)					
CKD 1	20(71.4)	8 (28.6)	1.05	0.39 - 2.81	0.928
CKD 2	24(75)	8 (25)	1.39	0.52 - 3.67	0.513
CKD 3a	3(50)	3(50)	0.38	0.07 - 2.04	0.352
CKD 3b	10(71.4)	4(26.6)	1.04	0.29 - 3.66	1.000
CKD 4	4(66.7)	2(33.3)	0.81	0.14 - 4.74	1.000
CKD 5	2(66.7)	1(33.3)	0..82	0.07 - 9.45	1.000
Age (mean + SD)	65.5 ± 13.7	61.6±16.5			0.159
Blood pressure					
SBP (mean + SD)	134.5 ± 33.7	131.3 ± 26.			0.573
DBP (mean + SD)	84.0 ± 21.8	85.9 ± 17.7			0.610
Serum UA levels (mean + SD)	8.4 ± 3.3	9.8 ± 3.3			0.020

Table 8: Clinical characteristics of mild-to-moderate and severe heart failure patients using LVEF1.

Characteristics	Mild to moderate HF	Severe HF	OR	CI at 95%	P value
Gender					
Females	65 (74.7)	22 (25.3)	1.58	0.79-3.15	0.197
Males	45 (65.2)	24 (34.8)	/	/	/
Level of Education					
None	26 (68.4)	12 (31.6)	0.88	0.39-1.94	0.746
Primary school	29 (65.9)	15 (34.1)	0.74	0.35-1.56	0.433
Secondary school	45 (75)	15 (25)	1.43	0.69-2.95	0.328
University	10 (71.4)	4 (28.6)	1.05	0.31-3.54	1.000

Table 9: Clinical characteristics of patients with mild-to-moderate and severe heart failure using LVEF 2.

Characteristics	Ajusted OR	CI at 95%	P ajusted
Myocardial disease	0.28	0.09 - 0.90	0.033
Serum UA levels	0.99	0.82 - 1.21	0.964
Decompensated HF	0.51	0.07 - 3.76	0.508
Chronic stable HF	1.58	0.27 - 11.53	0.632
NYHA class II	1.51	0.49 - 4.66	0.369
NYHA class IV	0.48	0.09 - 2.59	0.490

Table 10: Multivariate analysis between clinical parameters and severity using LVEF.

to 25mg/dl. Seventy-nine (42.2%) of the population had serum UA levels ranging between 6 and 8 mg/dl.

The mean age of heart failure patients with hyperuricemia was 64.23+/-14.25 years. Sixty (38.46%) were females and 61 (39.10%)

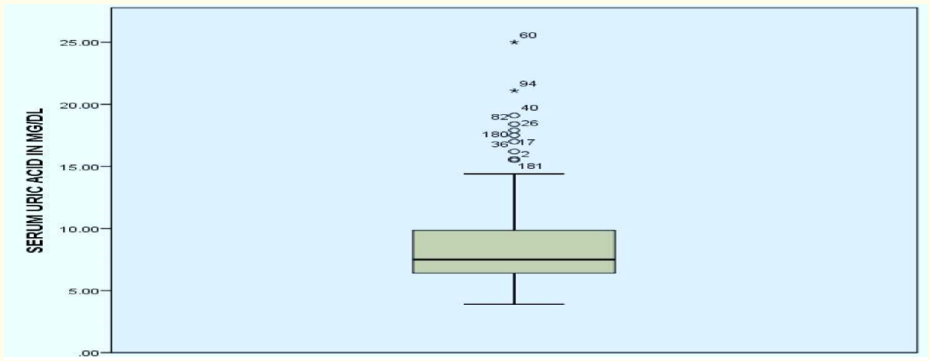

Figure 2: Serum uric acid levels in the study population.had a history of dyslipidaemia.

were males. Forty-six (29.49%) had secondary school education. Among these patients; 34 (21.80%) had acute HF, 18 (11.54%) had chronic decompensated HF and 69 (44.23%) had chronic stable heart failure. Forty (25.64%) were classified NYHA II and 32 (20.50%) were NYHA IV. Sixty-five (41.67%) had hypertension, 24 (15.38%) had diabetes, 14 (8.97%) had dyslipidaemia, 7 (4.48%) were smokers and 42 (26.92%) consumed alcohol. A hundred-and-fifteen (96.79%) were of normal weight. The mean systolic blood pressure and diastolic blood pressure of these participants were 132+/-33.17 and 84.66+/-20.74 mmhg. Forty-seven (30.13%) had myocardial disease, 39 (25%) had valvular heart disease and 26 (16.67%) had hypertensive heart disease. Thirty-seven (23.72%) had reduced ejection fraction. Forty-four (28.20%) were CKD 1-2.

		Normal SUA < 6	High SUA > 6	OR	CI	P
Diuretics n (%)	Yes	19 (16.1%)	99 (83.9%)	0.960	0.20 -4.73	1.000
	No	2 (16.7%)	10 (83.3%)			
Creatinine clearance (ml/ min/1.73m^2)		90.9	77.2			0.120

Table 11: Association between serum uric acid levels, creatinine clearance and diuretic use.

On bivariate analysis, hyperuricemia was associated to the following: gender (OR 0.78 95%CI 0.64-0.95 P value 0.023), acute HF (OR 7.03 95%CI 2.06-24.02 P value <0.001), chronic decompensated HF (OR 0.12 95%CI 0.04-0.40 P value <0.001), NYHA class IV (OR 6.47 95%CI 1.89-22.15 P value <0.001), preserved left ventricular ejection fraction (OR 0.46 95%CI 0.24-0.87 P value 0.018), reduced left ventricular EF (OR 3.14 95%CI 1.30-7.58 P value 0.006), myocardial heart disease (OR 2.8 95%CI 1.29-6.15 P value 0.005) and diabetes (OR 1.60 95% 1.41-1.82 P value<0.001). On multivariate analysis, gender was significantly associated to hyperuricemia (adjusted OR 0.43, 95%CI 0.18-0.99, adjusted P value 0.049).

Characteristics	Ajusted OR	CI at 95%	P adjusted
Sex	0.43	0.18-0.99	0.049
Acute HF	0.63	0.04-10.10	0.746
Chronic stable HF	0.54	0.08-3.41	0.509
NYHA class IV	3.45	0.51-23.50	0.205
Preserved LEVF	0.47	0.19-1.18	0.107
Reduced LEVF	1.01	0.27-3.69	0.992
Myocardial disease	2.46	1.01-5.99	0.047

Table 12: Multivariate analysis between clinical parameters and hyperuricemia.

Association between Serum uric acid levels and the severity of heart failure

Serum uric acid levels and NYHA association classification

There was a significant association between serum UA levels and NYHA classification of severity (OR 0.39, 95%CI 0.16-0.96, P value 0.035). Seventy-three (45.3%) of patients with HU had mild-to-moderate HF, while 88 (54.7%) with HU had severe HF. There was no significant association between serum uric acid levels and left ventricular ejection fraction classification (OR 0.24, 95%CI 0.05-1.07, p value 0.060).

SUAL mg/dl	High SUA	Low SUA	P value
Preserved EF	63(80.8%)	15(19.2%)	
Mid-range EF	23(92.2%)	2(8.0%)	0.232
Reduced EF	43(95.6%)	2(4.4%)	0.022

Table 13: Biv ariate analysis between serum uric acid levels and classification of left ventricular ejection fraction.

Sociodemographic and clinical profile of our participants

The age of patients with heart failure is usually between 64 and 77 years [37,38]. In our study, the mean age of participants was

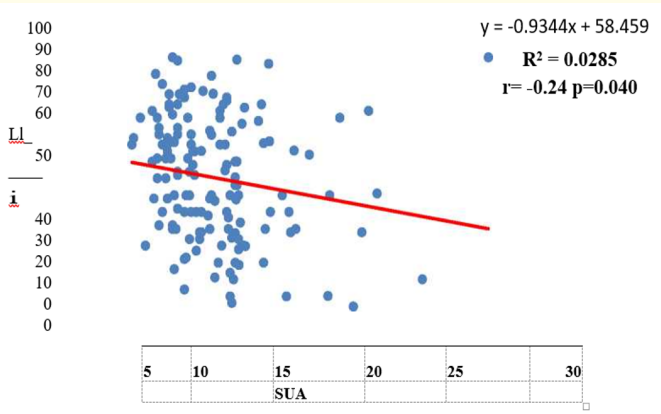

Figure 3: Correlation between left ventricular ejection fraction and serum UA level.

64.81 years with extremes of 21 to 96 years. This was similar to mean age of patients with heart failure in Indonesia in a study done by Siswanto., *et al.* which was 60 years [39]. It was also close to the mean age of heart failure patients in the study of Boombhi., *et al.* done in Yaounde-Cameroon, which was 61.46 years [16]. More than half of our population was females (54%) with a male to female ratio of 1:1.17. This was similar to the results of the European survey of heart failure patients in 2003, in which females accounted to more than half of the population (51%) [40]. The aetiologies of heart failure in our study were mainly myocardial heart diseases in 54.5%, Valvular heart diseases in 51.5% and hypertensive heart diseases in 8.5%. This was similar to the findings of the largest sub-Saharan heart registry, in which heart failure was mainly due to: cardiomyopathies, Valvular diseases and hypertensive heart diseases [37]. Serum uric acid levels in our population.

More than half of our general population had hyperuricemia (56.6%), with extremes of 3.9 to 25mg/dl. The mean serum uric acid level in our general population was 8.56 +/- 3.20 mg/dl and most patients (42.2%) had their serum uric acid level varying between 6 and 8 mg/dl. The prevalence of hyperuricemia in our general population was comparable to the prevalence of hyperuricemia in other diseases such as in ischemic stroke (58.8%) in the study of Mapoure., *et al.* [41]. The prevalence of hyperuricemia in patients with chronic decompensated heart failure in our study was 95% whereas their mean serum uric acid level was 11.35 +/- 4.42 mg/dl. This value was in accordance with the results of Muthiah., *et al.* in the US in 2014, where serum uric acid values were 9.1 +/- 2.8 mg/dl [42].

Serum uric acid and the severity of heart failure

Increased serum uric acid levels have been constantly been reported in patients with heart failure, and clinical data supports the possibility that uric acid levels provide prognostic information alone or in combination with other indicators of heart failure severity. Numerous studies reported that hyperuricemia indicated all-cause mortality in patients with heart failure. High serum uric acid levels has also been associated to long-term adverse outcomes and morbidity in patients with heart failure [43-45].

In our study, serum uric acid level was significantly higher in severe heart failure patients with NYHA III and IV. Of hyperuricemic patients, 54.6% were NYHA III-IV and 29.73% had serum uric acid levels greater than 8mg/dl. The mean serum uric acid level of patients with NYHA III/IV was higher compared to the mean serum uric acid levels of patients with NYHA I/II. Again, hyperuricemia was associated with NYHA III/IV (OR 0.39, 95%CI 0.160.96, P value 0.035). Our results were in accordance with the study of Adnan K., *et al.* in Pakistan in 2017, in which 47.02% of hyperuricemic patients were NYHA III/IV, with 34.93% having uric acid levels greater than 8 mg/dl [46]. As in our study, mean serum uric acid levels increased significantly with NYHA class [46].

Conclusion

At the end of this study we can conclude that More than half of patients with heart failure have hyperuricemia. Cardiovascular risk factors such as: hypertension, diabetes, dyslipidaemia, smoking and alcohol use is commoner in patients with heart failure and hyperuricemia. Serum uric acid has a significant correlation with established markers of severity, though this is more significantly associated with ejection fraction than NYHA classification. The higher the serum uric acid level, the more severe the heart failure.

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