

## Original Research Article


# Uric acid level as a biomarker in heart failure patients in a rural population attending tertiary care hospital in Chengalpattu District, Tamil Nadu

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	International Archives of Integrated Medicine, Vol. 7, Issue 12, December, 2020.	
	Available online at <a href="http://iaimjournal.com/">http://iaimjournal.com/</a>	
	ISSN: 2394-0026 (P)	ISSN: 2394-0034 (O)
	Received on: 14-11-2020	Accepted on: 05-12-2020
	Source of support: Nil	Conflict of interest: None declared.
<b>How to cite this article:</b> C.N. Sai Vigneshvar, E. Arumugam, S. Appandraj. Uric acid level as a biomarker in heart failure patients in a rural population attending tertiary care hospital in Chengalpattu District, Tamil Nadu. IAIM, 2020; 7(12): 57-63.		

## Abstract

**Introduction:** It is all around accepted that Heart Failure is a complex clinical condition that can result from any structural or functional cardiovascular issues that hinder the capacity of ventricles to fill up with or eject blood. Coronary artery disease represents a significant part of patients with chronic Heart failure. Heart failure is the end phase of all diseases of the heart and is a significant reason for morbidity and mortality.

**Aim of the study:** To analyze the serum uric acid level in heart failure patients.

**Materials and methods:** It was a retrospective conducted in the General Medicine and Cardiology Department of Karpaga Vinayaga Medical College, Chengalpattu district, Tamil Nadu from January 2020 to April 2020. The study was conducted on all patients with documented evidence of heart failure and heart failure treatment for at least one month. Patients of both sex aged between 20 to 80 years, patients with Heart failure both with preserved and decreased EF, and patients with Heart failure of at least 1-month duration were included in our study. The privacy and confidentiality of the patient were maintained. Informed consent was taken from the patient for the study.

**Results:** The mean age of the participants was 56.08±8.48 years. The age ranges from 43 years to 76 years. An equal number of males and females participated in our study. Overall co-morbidities present were CAD (62%), RHD (28%), and COPD (10%). Diabetes and hypertension were found among 80% and 78% respectively. Smoking was found among 42% and alcohol among 26% respectively. NYHA

grading was done, there were 28% in grade 2 followed by 62% in grade 3 and 10% in grade 4. Dyslipidemia was found among 48% of study participants. The mean uric acid levels were 7.12 mg.

**Conclusion:** It has been observed that in a clinical condition like hypoxemia there is an increase in the serum Uric acid level. The objective of our study was to find out the relationship between serum uric acid levels in the severity of Heart failure.

## Key words

Heart failure, Hyperuricemia, Uric acid.

## Introduction

It is all around accepted that Heart Failure is a complex clinical condition that can result from any structural or functional cardiovascular issues that hinder the capacity of ventricles to fill up with or eject blood [1]. Coronary artery disease represents a significant part of patients with chronic Heart failure. Heart failure is the end phase of all diseases of the heart and is a significant reason for morbidity and mortality. Heart failure is a thriving issue around the world. The predominance of cardiovascular disease increases with age. Heart failure is related to rising levels of Brain Natriuretic Peptide (BNP) and different markers like Uric corrosive, Troponin T and I, C-Reactive Protein, TNF Receptors, E-Selectin, and so forth [2-4]. Hyperuricaemia is normal in cardiovascular disease and has been related to poorer outcomes. Different lines of evidence propose that uric acid may have an immediate role in the pathogenesis of hypertension and vascular disease. Various examinations bolster that serum uric acid levels fill in as an amazing biomarker or autonomous predictor of prognosis and outcome in certain renal and cardiovascular diseases [5]. Some experimental trials exhibit that uric acid isn't inactive however may have both beneficial functions (acting as an antioxidant) and impeding activities (to invigorate vascular smooth muscle cell proliferation and instigate endothelial dysfunction) [6]. Hyperuricaemia is likewise connected with pernicious effects on endothelial dysfunction, oxidative metabolism, platelet adhesiveness, hemorheology, and aggregation [7]. There has been demonstrated an amazing and free prognostic estimation of uric acid levels in cardiovascular diseases. Studies have

indicated that uric acid is independently connected with Left Ventricular Mass Index and propose that the combination of hyperuricemia combined with left ventricular hypertrophy is an independent and ground-breaking indicator for cardiovascular illness [8]. Raised uric acid levels are related to diastolic dysfunction in congestive heart failure. Xanthine oxidase inhibition in patients with congestive heart failure may hypothetically bring about an improvement of diastolic capacity. In certain studies, when added to a far-reaching multi-parameter cardiovascular heart failure severity score, uric acid levels autonomously anticipated negative cardiovascular outcomes. As Heart failure is the main source of mortality, the capacity to foresee guess is basic for the ideal distribution of treatment. Biomarkers offering prognostic data are utilized in practice. Studies have indicated that separated from Brain Natriuretic Peptide as a biomarker, Uric acid is found to have prognostic incentive as well [9]. Increased Serum Uric acid in cardiovascular occasions might be an outcome of the hindrance of vascular Nitric Oxide, attributable to the capacity of Nitric Oxide to adjust Uric acid levels through its impact on Xanthine Oxidase. Initiation of Xanthine Oxidase through free radical release causes leucocyte and endothelial cell activation. Increases in Uric acid are related to increased vascular tone and depressed myocardial contractility using an increase in Xanthine Oxidase activity [10]. Therefore Uric acid could be related to hemodynamic compromise in heart failure. Our current study aims to evaluate serum uric acid levels in patients with heart failure and to correlate serum uric acid levels with morbidity and mortality in patients with heart failure.

## Materials and methods

This was a cross-sectional study conducted in the General Medicine and Cardiology Department of Karpaga Vinayaga Medical College, Chengalpattu district, Tamil Nadu from January 2020 to April 2020. The study was conducted on all patients with documented evidence of heart failure and heart failure treatment for at least one month. Patients of both sex aged between 20 to 80 years, patients with Heart failure both with preserved and decreased EF, and patients with Heart failure of at least 1-month duration were included in our study. Patients with pre-existing gout and heart failure, patients on long-standing diuretics and heart failure, chronic kidney disease, hematological malignancy, ATT – Pyrazinamide were excluded from the study. Institutional ethical committee approval was obtained for this study. The privacy and confidentiality of the patient were maintained. Informed consent was taken from the patient for the study. A detailed physical examination was conducted to assess patients' volume status (rales, edema, jugular venous distension), weight, height, body mass index, and orthostatic blood pressure changes. Complete blood count, blood glucose (fasting and 2-hour postprandial), fasting serum lipid profile, blood urea, serum creatinine were measured in all patients. Two-dimensional echocardiography was done in the cardiology department for all patients. Serum uric acid levels were measured on admission for all the 50 patients who met the inclusion criteria. All patients with documented evidence of heart failure and on heart failure treatment for at least one month were recruited for the study. Patient history was collected by a structured pro-forma which includes general details of the patient, any illness history, and present complaints. All the data (like anthropometric measurements and clinical data) collected were also noted.

## Statistical analysis

Descriptive statistics were reported as mean (SD) for continuous variables, frequencies (percentage) for categorical variables Data were statistically evaluated with IBM SPSS Statistics

for Windows, Version 20.0., IBM Corp., Chicago, IL.

## Results

Demographics were described in **Table - 1**. The mean age of the participants was  $56.08 \pm 8.48$  years. The age ranges from 43 years to 76 years. An equal number of males and females participated in our study. Overall co-morbidities present were CAD (62%), RHD (28%), and COPD (10%). Diabetes and hypertension were found among 80% and 78% respectively. Smoking was found among 42% and alcohol among 26% respectively. NYHA grading was done, there were 28% in grade 2 followed by 62% in grade 3 and 10% in grade 4. Dyslipidemia was found among 48% of study participants. The mean uric acid levels were 7.12 mg/dL.

The co-morbid factors such as CAD, RHD didn't show any statistical significance but COPD was seen more among elevated serum uric acid levels ( $p=0.04$ ). Similarly, diabetes and hypertension were seen more among elevated serum uric acid levels ( $p=0.001$ ). Associated factors like smoking and alcohol were also seen more among elevated serum uric acid levels ( $p=0.001$ ). There was no association between NYHA grading and dyslipidemia among the elevated serum uric acid levels (**Table – 2**).

## Discussion

Raised serum uric acid levels have been related to an expanded risk for cardiovascular disease.<sup>11</sup> Serum uric acid level is a record of oxidative stress in the human body [12]. Serum uric acid is known to add to endothelial dysfunction by hindering nitric oxide production [13]. Serum uric acid has additionally been demonstrated to be contrarily related to the proportions of functional capacity and maximal oxygen consumption. Among patients with chronic cardiovascular dysfunction, serum uric acid concentrations are related to the more prominent movement of superoxide dismutase and endothelium-subordinate vasodilatation [14].

Another potential pathophysiological interface among hyperuricemia and cardiovascular dysfunction may be through inflammation. Asymptomatic hyperuricemia is a proinflammatory state related to more significant levels of serum markers of inflammation, for example, C-responsive protein, interleukin-6, and neutrophil count [15, 16, 17].

**Table – 1:** Demographics.

Variable	Frequency	Percentage
Gender		
Male	25	50
Female	25	50
CAD	31	62
RHD	14	28
COPD	5	10
CALCIFIC AS/AR	21	42
DM	40	80
HTN	39	78
Smoking	21	42
Alcohol	13	26
NYHA		
Grade 2	14	28
Grade 3	31	62
Grade 4	5	10
Dyslipidemia	24	48

**Table - 2:** Demographic characteristics by patients with or without elevated uric acid (n=50).

Variable	≤ 6 mg/dL (n=21)	≥ 6 mg/dL (n=29)	p value
Age	55.57±8.32	56.45±8.72	0.72
Gender			
Female	18 (85.7)	7 (24.1)	<0.001
Male	3 (14.3)	22 (75.9)	
CAD	12 (57.1)	19 (65.5)	0.57
RHD	9 (42.9)	5 (17.2)	0.04
COPD	0	5 (17.2)	0.04
CALCIFIC AS/AR	9 (42.9)	12 (41.4)	0.91
Duration in months	7.14±2.15	8.59±1.93	0.02
DM	12 (57.1)	28 (96.6)	0.001
HTN	14 (66.7)	25 (86.2)	0.16
Smoking	3 (14.3)	18 (62.1)	0.001

Alcohol	0	13 (44.8)	0.001
NYHA			
Grade 2	4 (19)	10 (34.5)	0.28
Grade 3	16 (76.2)	15 (51.7)	
Grade 4	1 (4.8)	4 (13.8)	
Dyslipidemia	8 (38.1)	16 (55.2)	0.30

Among patients with heart failure, hyperuricemia is related to more elevated levels of markers of endothelial activation, for example, the soluble intercellular adhesion molecule 1, and inflammatory markers, for example, interleukin-6, tumor necrosis factor- $\alpha$ , and its receptors. Comparable observations have been made in some population-based studies [18] and clinic-based investigations. The danger of cardiovascular breakdown was proportionate to the level of raise [19] of serum uric acid levels among patients with gout [20]. Locally, in any event, when there is no active joint inflammation, the synovial liquid of patients with gout shows low-grade inflammatory activity [20]. Increased degrees of serum uric corrosive among ordinary people anticipate hypertension, renal dysfunction, and coronary artery disease and predict reduced life expectancy [21]. Lowering of serum uric acid with allopurinol can diminish blood pressure among hypertensives [20, 21]. This raises the chance of the hyperuricemia-heart failure to connect being mediated by hypertension, a theory that can't be straightforwardly tried in observational investigations. We have studied 50 patients with heart failure. These patients were admitted to our hospital from January 2020 to April 2020. Their comparative uric acid levels are given in the table above. The mean age of the participants was 56.08±8.48 years. The age ranges from 43 years to 76 years. An equal number of males and females participated in our study. Overall co-morbidities present were CAD (62%), RHD (28%), and COPD (10%). Diabetes and hypertension were found among 80% and 78% respectively. Smoking was found among 42% and alcohol among 26% respectively. NYHA grading was done, there were 28% in grade 2

followed by 62% in grade 3 and 10% in grade 4. Dyslipidemia was found among 48% of study participants. The mean uric acid levels were 7.12 mg/dL. This is in concordance with the investigation done by Tuomilhto, et al. [22] in which there was no critical relationship between serum uric acid level and diabetic levels. Dyslipidemia was available in 71% of the people and it was missing in 29% of the people. There was no noteworthy distinction in serum uric acid levels concerning the presence and absence of dyslipidemia. The co-morbid factors such as CAD, RHD didn't show any statistical significance but COPD was seen more among elevated serum uric acid levels ( $p=0.04$ ). Similarly, diabetes and hypertension were seen more among elevated serum uric acid levels ( $p=0.001$ ). Associated factors like smoking and alcohol were also seen more among elevated serum uric acid levels ( $p=0.001$ ). There was no association between NYHA grading and dyslipidemia among the elevated serum uric acid levels. Henceforth we derived that likely uric acid isn't only a marker however it has a causative factor too. Anyway because of the presence of co-morbid ailments which likewise impact the uric acid levels, this couldn't be speculated. The perceptions that we have made recommend a role for primary prevention in heart failure. In any case, the existing literature is clashing on whether a decrease in serum uric acid will bring about quantifiable clinical advantage among those with established heart failure [23, 24]. Some studies have even indicated that that increased serum uric acid brought about by diuretic use may have a helpful job in itself [25]. On the other hand, the Losartan Intervention For Endpoint decrease in hypertension (LIFE) study has discovered that the uricosuric property of Losartan, has an advantageous impact among patients with hypertension and left ventricular remodeling and hypertrophy [24, 26]. The components by which uric acid reduction treatment is valuable is still not clear. In particular, it is hazy whether the notified advantage from the utilization of xanthine oxidase inhibitors intercedes [27] through a decrease in serum uric acid levels or

some other mechanism. Restraint of xanthine oxidase enzyme by allopurinol has helpful impacts regarding improved peripheral vasodilator capacity, systemic blood flow, and clinical outcomes [28, 29]. Randomized controlled studies are additionally unclear about the possible advantages of allopurinol or its metabolite oxypurinol on heart failure. The La Plata study demonstrated an improvement in the left ventricular launch part with the utilization of allopurinol [30] however the Oxypurinol Therapy for Congestive Heart Failure (OPT-CHF) study didn't show any benefits overall [31]. Our study had certain restrictions. Our example size was small. Also, patients were followed for just thirty days, and expanding the term of follow up to in any event a half year or one year would have given a superior evaluation of contrasts in mortality pattern. In outline, our study found that hyperuricemia is related to a more prominent frequency of heart failure and hyperuricemia is an indicator of all reason mortality in patients with heart failure. Future investigations utilizing different urate reduction treatment methodologies would be expected to decide if the essential counteraction of heart failure is conceivable. As the commonness of heart failure is increasing, even a little clinical advantage got from such investigations can be of gigantic benefit to the community.

## Conclusion

It has been observed that in a clinical condition like hypoxemia there is an increase in the serum Uric acid level. The objective of our study was to find out the relationship between serum uric acid levels in the severity of Heart failure.

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