International Journal of Research in Medical Sciences
Sharma S et al. Int J Res Med Sci. 2025 Jan;13(1):265-270
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20244125

Original Research Article

Prognostic role of serum uric acid levels in patients with decompensated chronic heart failure

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Received: 12 November 2024
Revised: 13 December 2024
Accepted: 20 December 2024

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ABSTRACT

Background: Chronic heart failure (CHF) affects over 26 million people worldwide and is characterized by the heart's inability to meet the body's metabolic demands due to structural or functional abnormalities, resulting in high morbidity and mortality. Traditional biomarkers such as sST2, cardiac troponin, and natriuretic peptides are costly and not universally accessible, creating a need for affordable and accessible alternatives.
Methods: This study evaluated the prognostic role of serum uric acid levels in decompensated CHF by comparing outcomes such as hospitalization duration, ICU stay, and mortality between patients with high (>7 mg/dl) and low (≤7 mg/dl) uric acid levels. Conducted over 14 months at K.P.S. Post Graduate Institute, GSVM Medical College, Kanpur, the study included 126 patients selected through purposive sampling. Data collection involved physical exams, laboratory tests, echocardiography, and ECGs.
Results: Elevated serum uric acid levels were associated with reduced ejection fraction, prolonged hospital and ICU stays, and worse cardiac function. Patients with higher uric acid levels demonstrated poorer clinical outcomes, highlighting its potential role in risk stratification and prognosis.
Conclusions: Serum uric acid is a valuable, low-cost prognostic marker for CHF, offering potential utility in early diagnosis and management. Its incorporation into clinical practice could improve outcomes and facilitate timely, affordable interventions, addressing the growing global burden of CHF. These findings underscore the need for further research to explore its integration into clinical workflows.

Keywords: Chronic heart failure, Decompensated CHF, Mortality, Prognostic marker, Serum uric acid

INTRODUCTION

Chronic heart failure (CHF) is a serious global health concern, with a prognosis worse than that of bladder cancer in men and breast cancer in women. Over 26 million people worldwide are impacted by this complicated clinical entity, which is typically characterized as a heart's failure to meet necessary metabolic demands and the perfusion of organs and tissues due to structural or functional cardiac abnormalities.[1]

Numerous biomarkers have previously been studied in the context of HF. Thus far, soluble suppression of tumorigenicity-2 (sST2), cardiac troponin, and natriuretic peptides have been identified as valuable biomarkers for HF diagnosis, risk assessment, and prognosis. The Heart Failure Association of the European Society of Cardiology (ESC) consensus statement now recommends a multi-marker approach that incorporates the biomarkers mentioned above, based on the available data. However, these are associated with high costs and are not easily available in many healthcare settings.

Uric acid is linked to heart failure through mechanisms involving oxidative stress, inflammation, endothelial dysfunction, renal impairment, direct myocardial effects, neurohormonal activation, and its association with metabolic syndrome. Understanding these links highlights the potential of serum uric acid as a prognostic marker for heart failure and suggests that managing uric acid levels could be beneficial in the treatment and prognosis of heart failure patients.[2,3]

Objective

To compare the duration of hospitalization, duration of ICU stay, and mortality in two groups of patients with decompensated chronic heart failure having high uric acid levels (>7 mg/dl) and low uric acid levels (≤7 mg/dl).

METHODS

Study design and setting

It was a comparative observational study that took place at LLR and associated hospitals, KPS Postgraduate Institute of Medicine, GSVM Medical College, Kanpur.

Study duration

The study was conducted for 14 months from May-2023 to June-2024.

Study population

126 patients admitted at KPS Post Graduate Institute of Medicine, GSVM Medical College, Kanpur with chronic heart failure during the duration of the study.

Inclusion criteria

Patients admitted with symptoms and signs of heart failure. Age group of both sexes >18 years.

Exclusion criteria

Recent surgery or trauma, endocrine disorders: hypothyroidism, hyperparathyroidism, acidosis (lactic/ketoacidosis), pregnancy gout, chronic kidney disease, malignancies (including those on chemotherapy). Specific diseases: Paget disease, polycythemia vera, hemolysis, tuberculosis, sarcoidosis, Down's syndrome. Drug use: Allopurinol, febuxostat, ethambutol, pyrazinamide, cyclosporin, niacin.

Data collection and study tool

A structured questionnaire was developed to collect detailed clinical and demographic information, including the duration of heart failure, symptoms (e.g., dyspnea, fatigue), prior treatments (e.g., medications), associated comorbidities (e.g., diabetes, hypertension), and lifestyle factors such as smoking and alcohol use. The questionnaire was informed by methodologies used in similar studies, such as those by Wasserman et al, Car et al, and Çengel et al, which utilized clinical assessments and NYHA classifications to stratify symptom severity.[10-12] The NYHA classification system, as recommended by Ponikowski et al in the ESC guidelines, was employed to assess symptom burden and functional capacity.[1]

The questionnaire was reviewed by a panel of three cardiologists to ensure content validity and pretested on a pilot group of 10 patients for clarity and feasibility. Revisions were made based on feedback to improve the tool's comprehensiveness and usability. Responses were categorized as binary (e.g., comorbidities: present/absent) or ordinal (e.g., NYHA classification: I-IV). This structured approach ensured standardization and facilitated statistical analysis.

A detailed physical examination was conducted to assess patients' volume status (rales, edema, jugular venous distension), and orthostatic blood pressure changes. Complete blood count, blood glucose (fasting and 2 hours post prandial), fasting serum lipid profile, blood urea, serum creatinine, and serum electrolytes 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 126 patients who met the inclusion criteria. Patients were followed up for a period of hospital stay and prognosis was assessed by noting down duration of hospital stay or mortality.

Data analysis

Data analysis was done using licensed SPSS software version 21.0. Data is presented in the form of tables and appropriate diagrams. Qualitative data was summarized as proportions while quantitative data is as mean, median, and appropriate measures of dispersion including confidence intervals.

Quantitative data was analysed using paired t-test and qualitative data by Chi-square/fisher exact test with a value of $p<0.05$ was taken as significant. Survival analysis was done by using Kaplan-Meier curves, log-rank test and Cox regression. Logistic regression analysis identified predictors of mortality, calculating crude and adjusted odds ratios (OR) for various independent variables, such as high uric acid levels, gender, and comorbidities.

Ethical consideration

Ethical clearance was obtained from the Institute Ethics Committee of GSVM Medical College, Kanpur, Uttar Pradesh. Each eligible subject was explicitly explained about the purpose of the study by the investigator and informed written consent was obtained from all adult participants before inclusion, for participants >12 years assent was taken.

RESULTS

Table 1 data reveals significant differences between participants with high and low uric acid levels. Those with high uric acid are associated with NYHA grade IV, have lower ejection fractions, require ICU stays, and experience higher mortality rates, all with p values of 0.000. Non-significant differences include age distribution, gender, and most causes of chronic heart failure, such as coronary artery disease and rheumatic heart disease, with p values greater than 0.05. Co-morbidities and risk factors like diabetes mellitus, hypertension, smoking, alcohol consumption, dyslipidaemia, and diuretic use also showed no significant differences between the groups. In summary, high uric acid levels are linked to more severe NYHA classifications, lower ejection fractions, increased ICU stays, and higher mortality, while other factors such as age, gender, and co-morbidities remain similar across groups.

Table 1: Association between high and low uric acid with different variables.

Variables	High uric acid	Low uric acid	χ^2 value	P value
N (%)				
Age (in years)				
≤20	2 (66.67)	1 (33.33)	10.63	0.153#
21-30	7 (63.64)	4 (36.36)		
31-40	7 (70.00)	3 (30.00)		
41-50	4 (28.57)	10 (71.43)		
51-60	17 (38.64)	27 (61.36)		
61-70	19 (57.58)	14 (42.42)		
71-80	6 (75.00)	2 (25.00)		
81-90	1 (33.33)	2 (66.67)		
Sex				
Male	37 (49.33)	38 (50.67)	0.03	0.550
Female	26 (50.98)	25 (49.02)		
NYHA				
Grade III	10 (15.38)	55 (84.62)	64.35	0.000
Grade IV	53 (86.89)	8 (13.11)		
Cause of CHF				
Coronary artery disease	30 (50.00)	30 (50.00)	0.50	1
Rheumatic heart disease	12 (60.00)	8 (40.00)	0.95	0.329#
COPD- Cor Pulmonale*	9 (56.25)	7 (43.75)	0.286	0.593
Calcified AS/AR^	0	4 (100)	4.131	0.119#
Eisenmenger syndrome	3 (100)	0	3.073	0.244#
Dilated cardiomyopathy- unknown cause	6 (46.15)	7 (53.88)	0.08	0.770
Alcoholic cardiomyopathy	3 (30.00)	7 (70.00)	1.738	0.187
Ejection fraction				
15-20	10 (83.33)	2 (16.67)	34.91	0.000#
21-25	19 (82.61)	4 (17.39)		
26-30	4 (40.00)	6 (60.00)		
31-35	15 (57.69)	11 (42.31)		
36-40	7 (46.67)	8 (53.33)		
41-45	7 (36.84)	12 (63.16)		
46-50	1 (10.00)	9 (90.00)		
51-55	-	11 (100)		
Co-morbidities/ risk factors				
Diabetes mellitus	27 (54.00)	23 (46.00)	0.531	0.466
Hypertension	24 (48.00)	26 (52.00)		
Smoking	24 (61.54)	15 (38.46)		
Alcohol consumption	19 (50.0)	19 (50.00)		
Dyslipidaemia	30 (60.00%)	20 (40.00)		
Diuretic use	30 (56.60)	23 (43.40)		
ICU Stay	29 (93.55)	2 (6.45)	31.19	0.000#
Mortality	17 (94.40)	1 (5.60)	16.60	0.000#

*Significant, #Non-significant

Table 2: Median survival rate in both groups in hospital and ICU administration.

	High uric acid	Low uric acid	T-value	P value
Hospital stays				
p50 (median) (days)	7	5	5.45	0.000
ICU Stay				
p50 (median) (days)	4	3.5	6.39	0.000

Table 3: Survival rate at the end of 7 and 10 days in both groups.

	High uric acid	95% CI	Low uric acid	95% CI
At 7 days	79.97%	65.55-88.85	96.30%	76.49-99.47

Table 4: Log rank association between observed and expected events in both groups.

Log rank	Observed	Expected	χ^2 value	P value
High uric acid	17	13.60	4.00	0.045
Low uric acid	1	4.4		

Table 2 data indicates significant differences in hospital and ICU stays between participants with high and low uric acid levels. The median hospital stay for participants with high uric acid was 7 days compared to 5 days for those with low uric acid, with a t-value of 5.45 and a p value of 0.000. Similarly, the median ICU stay was 4 days for participants with high uric acid and 3.5 days for those with low uric acid, with a t-value of 6.39 and a p value of 0.000. These findings highlight that participants with high uric acid levels tend to have longer hospital and ICU stays.

Table 3 shows survival rates on different days with high and low uric acid levels. The survival of those with high uric acid was near 80 percent at the end of the week and it declined to 55 percent at 10 days. While the survival of those with low uric acid levels remained constant at 96 percent.

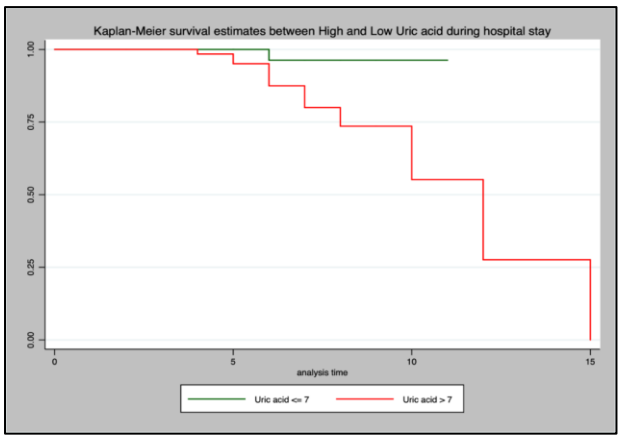

Figure 1: Kaplan-Meier survival estimates in both groups during hospital stay.

Table 4 illustrates the comparison between observed and expected events in both groups, revealing significant deviations. The observed frequencies differ markedly from the expected frequencies, indicating that the actual distribution of events does not fit the predicted model.

Figure 1 is the Kaplan-Meier survival estimate graph which reveals that hospitalized patients with uric acid levels greater than 7 mg/dl exhibit significantly lower survival probabilities compared to those with levels less than or equal to 7 mg/dl. Throughout the hospital stay, patients with lower uric acid levels maintain a stable and high survival rate, while those with higher levels experience a notable decline in survival probability. This suggests that elevated uric acid levels are associated with an increased risk of mortality during hospitalization.

DISCUSSION

Elevated serum uric acid, a byproduct of purine metabolism, has been consistently linked to adverse outcomes in patients with chronic heart failure.[4] This association stems from uric acid's contribution to oxidative stress, endothelial dysfunction, and inflammation, all of which exacerbate heart failure progression.[5] Furthermore, impaired renal function, common in decompensated heart failure, further elevates uric acid levels, creating a vicious cycle of worsening cardiac and renal dysfunction.[6]

Our study of 126 participants, with an equal distribution of high and low uric acid levels, offers further insights into this relationship. While the mean age of participants with high uric acid (53.75 years) was slightly lower than those with low uric acid (54.94 years), median ages (58 and 56 years, respectively) and a broader interquartile range for the high uric acid group suggest a trend towards higher uric acid levels in older patients. This finding aligns with previous research by Anker et al, which reported a mean age of 59±12 years in their study population.[7]

Interestingly, our study found an equal distribution of high and low uric acid levels between genders, with a slight

majority being male (59.52%). This contrasts with previous studies that observed a male preponderance, suggesting that gender may not significantly influence uric acid levels in our cohort of CHF patients.[7,8]

Our analysis of age distribution revealed a potential age-related trend in uric acid levels. The 51-60 and 61-70 age groups exhibited the highest prevalence of high uric acid, while the 41-50 age group had a higher prevalence of low uric acid. This suggests that middle-aged adults (51-70 years) may be more susceptible to elevated uric acid levels.

Our analysis revealed that those with high uric acid levels experienced significantly longer hospital (mean: 7.19 days) and ICU stays (mean: 3.83 days) compared to those with low uric acid levels (mean: 5.33 and 3.5 days, respectively). This difference highlights the increased severity and potentially more complex clinical management associated with elevated uric acid. Palazzuoli et al, conducted a study that hospitalized patients for heart failure with high serum uric acid needed rehospitalization at the end of six months.[9]

Most strikingly, we observed a significantly higher mortality rate in the high uric acid group (17 deaths) compared to the low uric acid group (1 death), a finding statistically significant ($p < 0.0001$). This result aligns with several studies, including those by Wassermann et al, Car et al, and Cengel et al, which all identified high serum uric acid as an independent predictor of mortality in similar patient populations.[10-12]

Our Kaplan-Meier survival estimates further underscore this association, demonstrating significantly lower survival probabilities for patients with uric acid levels above 7 mg/dl during their hospital stay. This finding is consistent with research by Ndreppa et al and Okazaki et al, which also reported higher mortality estimates and lower survival rates, respectively, in patients with elevated uric acid levels.[14]

The log-rank test confirmed a significant difference in mortality between the high and low uric acid groups ($p<0.05$), further strengthening the evidence for this association. These findings are consistent with a growing body of literature, including studies by Sakai et al, Anker et al, and Alimonda et al, which have all established a link between high uric acid levels and increased mortality risk in CHF patients.[7,8,15]

This study has some limitations. The small sample size (n=126) and single-centre design limit the generalizability of the findings. The short, one-month follow-up period restricts our ability to assess long-term patient outcomes. Additionally, the lack of readmission data and the potential for unmeasured confounders related to high serum uric acid may impact the robustness of the results.

CONCLUSION

This study demonstrates a strong association between elevated uric acid levels and adverse outcomes in patients with chronic heart failure, including severe heart failure, reduced ejection fractions, prolonged hospital and ICU stays, and increased mortality. The findings highlight the potential of serum uric acid as a valuable prognostic biomarker in this population. By comprehensively assessing various risk factors, such as diabetes, dyslipidemia, and long-term diuretic use, the study adds clinical relevance and depth to understanding the interplay of these factors in heart failure. Additionally, the focus on hospital stay duration provides important insights often overlooked in similar research.

Recommendations

While further studies are necessary to clarify the causal relationship between uric acid and heart failure outcomes, these findings suggest the potential benefits of targeted interventions to manage uric acid levels in affected patients. Exploring such strategies could lead to improved treatment approaches, particularly in the context of the rising prevalence of heart failure. Even modest advancements in management could significantly impact public health outcomes by reducing mortality and improving the quality of life for these patients.

ACKNOWLEDGEMENTS

We would like to thank our study participants who shared their valuable time and information.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sharma S, Priyadarshi BP, Sachan M. Prognostic role of serum uric acid levels in patients with decompensated chronic heart failure. Int J Res Med Sci 2025;13:265-70.