

Uric Acid as a Prognostic Marker in Heart Failure

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1. Introduction

Heart failure is a problematic disease in both developed and developing countries worldwide with more than 20 million people affected each year. In developed countries the prevalence is 2%. The prevalence rises with age, with 6-10% of people affected over the age of 65 years. Women contribute to 50% of patients, This can be due to long life expectancy. Overall prevalence is increasing, this can be contributed in part by new advanced therapies for cardiac disorders, coronary heart disease, rheumatic heart disease and arrhythmias that allows a longer survival. Heart failure patients are classified into heart failure with preserved ejection fraction and heart failure with reduced ejection fraction.

Numerous studies show increasing evidence of role of uric acid as a marker of metabolic and hemodynamic derangements in heart failure patients. Uric acid can also be used as a predictor of survival in these patients.

2. Aims and Objectives

To estimate the level of uric acid in heart failure patients and the prognostic importance of uric acid to be assessed and to identify the importance of uric acid as a prognostic marker in heart failure patients.

3. Materials and Methods

Source of Study

Data consists of primary data collected by the principal investigator directly from the patients who were admitted in Government Coimbatore Medical College and Hospital

Design of the Study

Prospective study

Period of Study

One year 2016- 2017

Sample Size

100 patients with heart failure

Inclusion Criteria

Patients above the age of 18 years with ejection fraction less than 55%.

Exclusion Criteria

- Patients with gout
- Patients with acute and chronic renal failure
- Patients with prior history of malignancy

- Patients not capable of giving consent (psychiatric patient)
- Patients not willing to participate in the study
- Pregnant and lactating women

Methodology

The study will be undertaken on the patients attending medicine inpatient department and admitted in Coimbatore medical college and hospital, Coimbatore during the study period 2016- 2017. A total of 100 patients with heart failure are included in the study based on the inclusion and the exclusion criteria.

The list of patients enrolled in the study is appended along with the dissertation. The study excludes minors, pregnant women, mentally ill and non volunteering patients.

- 1) The study is proposed to be conducted after obtaining informed consent from the patients. The duration of study is one year 2016- 2017. A detailed history, clinical examination and ECHO evaluation was done for all patients.
- 2) Blood sample was collected from patients and analysed by standard methods for blood sugar, urea and creatinine.
- 3) Serum uric acid to be analysed by automatic chemical analyser.
- 4) Significant differences between serum uric acid in different subgroups to be observed over a period of one year and role of uric acid as a prognostic marker to be evaluated.

4. Results

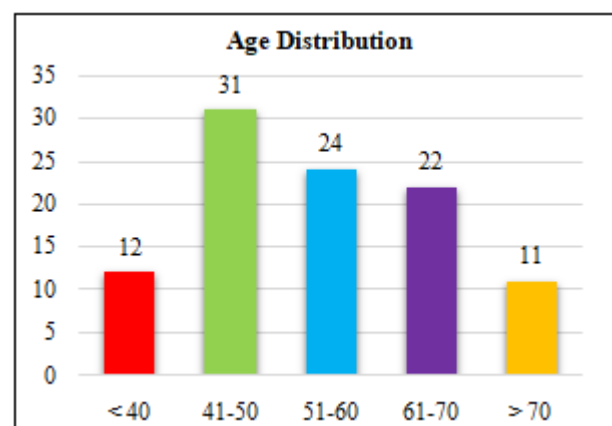


Chart 1: Age distribution in the study

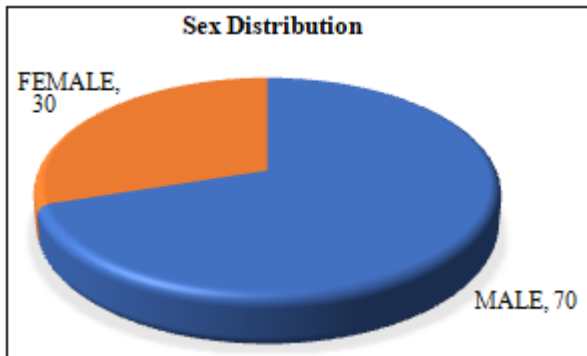


Chart 2: Sex distribution in the study

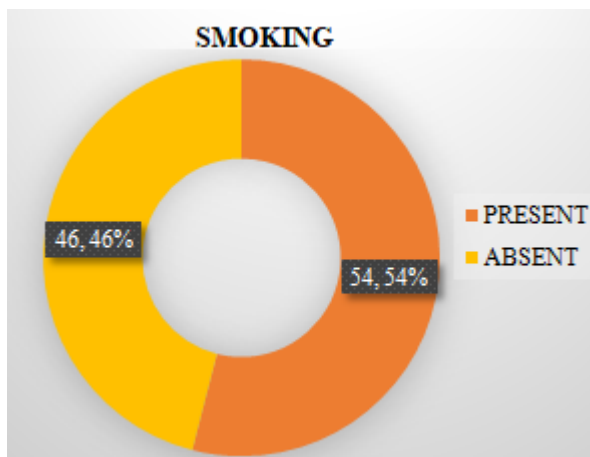


Chart 3: Distribution of smokers and non smokers in the study group

Serum Uric Acid and Age

This table shows the correlation of levels of uric acid and age. There is a significant correlation between increasing age and uric acid.

Table 16: Correlation between age and uric acid

Age (In Years)	Serum Uric Acid	
	High	Low
<40	2	10
41-50	15	16
51-60	13	11
61-70	18	4
>70	9	2
P VALUE - 0.002		
SIGNIFICANT		
KRUSKAL WALLIS TEST		

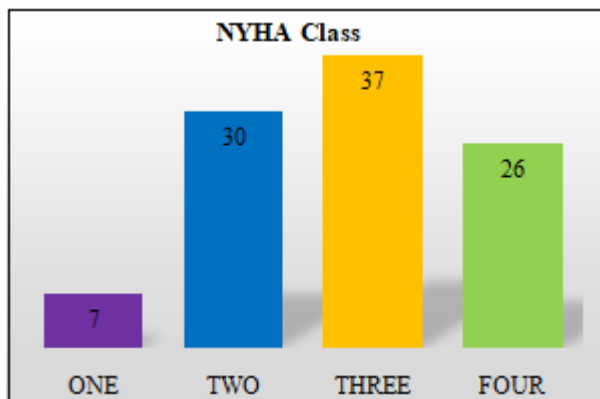


Chart 7: Distribution of patients based on NYHA

Classification of patients based on ejection fraction

38% of patients had an ejection fraction that is < 40%

Table 11: Patients grouping based on ejection fraction

Ejection Fraction	No of Patients	Percentage
< 40 %	38	38%
> 40 %	62	62%

Mean Ejection Fraction and Prognosis

This shows that the mean ejection fraction in patients who died was 30.5 %.

Table 40: Mean EF versus prognosis

Prognosis	Ejection Fraction	
	Mean	SD
Dead	30.5	1.4
Alive	41.5	5.3
p Value - 0.001		
Significant		
Unpaired T Test		

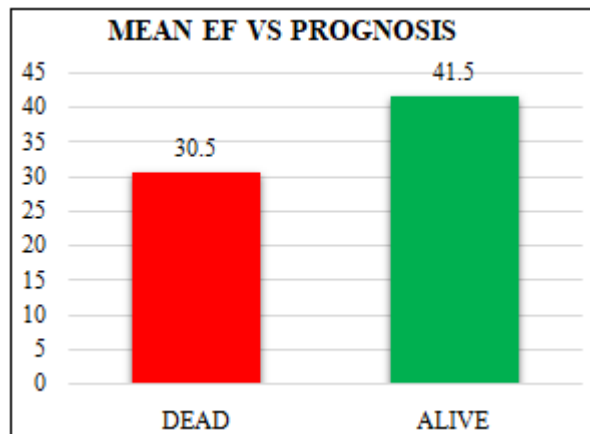


Chart 37: Mean EF versus prognosis

Prognosis versus Serum Uric Acid

Table 41: Correlation between uric acid and prognosis

Serum Uric Acid	Prognosis	
	Dead	Alive
> 6.8	13	44
< 6.8	3	40
P VALUE - 0.03		
ODDS RATIO - 4.75		
SIGNIFICANT		
CHI SQUARE TEST		

5. Discussion

In my study, patients with heart failure with EF <55% were taken and the association between uric acid and clinical symptoms, signs and various risk factors was analysed and observed over a period of one year. The role of hyperuricemia in the outcome of heart failure patients was also assessed. There are previous studies that uncovered the association of serum uric acid levels and the development of heart failure in population of patients with stable coronary heart disease. Even after accounting of multiple confounding factors the association was found to be significant. Mazza et al found that the relative risk of coronary heart disease death in elderly individuals with diabetes was elevated in patients

with highest and lowest levels of uric acid. Chang fu kuo et al in their study proved a definite evidence that describes the association of high uric acid levels and mortality, which was previously thought to be controversial. In my study it was found that there was a significant correlation between age and uric acid with a p value of 0.002 which was statistically significant. With increase in age of the patients the level of uric acid in serum was found to be increased.

On the other hand, a significant negative correlation was present between ejection fraction and serum uric acid levels. In my study hyperuricemia (uric acid level > 6.8 mg/dl) was found in 38 % of patients and 62% of patients had serum uric acid < 6.8 mg/dl. Serum uric acid levels and its correlation with sex of the individuals revealed no significance. Smoking also did not affect the uric acid levels significantly. Uric acid levels were assessed between diabetic and patients with no Diabetes Mellitus in my study. Totally 38% of patients had diabetes out of which 22 had high uric acid levels. 62 patients had no diabetes, among them 35 patients had high uric acid levels. There was no statistically significant correlation between diabetes and serum uric acid levels and the p value was 0.882. In this study, 39% of patients were hypertensive and 61% had no hypertension. It was found that difference between the mean uric acid levels in both groups was not significant.

In Apolipoprotein mortality risk study (AMORIS), moderate levels of serum uric acid were linked with increased incidence of acute myocardial infarction, stroke and HF in middle age subjects without CAD. AMORIS study implies that the association between uric acid and heart failure was not solely mediated by myocardial infarction, but other mediators present in CAD may be involved. Further mechanisms by which UA could be associated with heart failure in these persons includes an increased oxidative burden, increased endothelial dysfunction, a proinflammatory state, and subclinical atherosclerosis. Suggested variables were MI size and effect on left ventricular function. In my study patients were categorised into four groups based on New York Heart Association Classification (NYHA). Study exposed that there was significantly high serum uric acid levels in NYHA class III and IV patients. The mean serum uric acid in NYHA class III and IV patients was 7.38 mg/dl and 7.55 mg/dl respectively. In this study 38% of the individuals had an ejection fraction of < 40%. The low ejection fraction had significant negative correlation with high uric acid levels. The p value obtained by chi square test was 0.003. The mean uric acid in patients with low ejection fraction was 7.43 mg/dl.

In total number of patients, 16 patients died during the period of study. In patients with hyperuricemia the prognosis was worse with rise in mortality rates. The mean uric acid level in patients who died was 8.21 mg/dl as compared to 7.02 mg/dl in patients who survived. The p value was 0.034 and was significant. Several studies have shown an association between hyperuricemia in congestive heart failure and morbidity and mortality. Data from Beta Blocker Evaluation of Survival Trial took a different approach assuming that hyperuricemia without chronic renal failure is primarily due to increased production of UA from the failing

heart. The conclusion in that study was hyperuricemia was associated with poor outcomes in heart failure without renal failure. The correlation between low EF and prognosis was statistically significant with p value of 0.001. The mean EF in patients who died was 30.5%. The study exposed a significant increase in mortality with rise in age of the patient. In NYHA class III and IV patients the death of patients was high compared to class I and II. This was found to be significant with a P value of 0.001.

The study uncovered that sex, smoking, Diabetes mellitus and Hypertension did not affect the prognosis of heart failure patients significantly. Gotsman et al found in heart failure register based study that treatment with allopurinol in CHF improved survival rates significantly. Another retrospective study examined the effect of allopurinol on mortality and hospitalization in heart failure patients. It was found that high dose allopurinol (300 mg/day), a xanthine oxidase inhibitor was associated with an increased all cause mortality (p value - 0.05).

6. Conclusion

In my study hyperuricemia was observed in 38% of heart failure patients with EF <55%. It was observed that NYHA class III and IV patients had increased uric acid levels. There was significant negative correlation between low ejection fraction and uric acid. Hyperuricemia was associated with increased mortality rates. This clearly establishes the role of serum uric acid levels as a prognostic marker in heart failure patients. Regardless of whether uric acid levels are ready for clinical use, either as prognostic marker or diagnostic marker to find out the morbidity, complications and subsequent mortality in heart failure patients, with EF < 55% and specifically for NYHA III and IV heart failure with EF < 40%, the therapeutic intervention with uric acid reducers, xanthine oxidase inhibitors for the above ailment should be further explored with large multicentric, cross sectional, double blind control prospective study. As this pathway can be used as a novel therapeutic target, further prospective studies are needed to validate that routine measurements of uric acid and the reduction of uric acid levels in this group of heart failure patients alters the morbidity and mortality rates.

This particular study is a single centric prospective study done in a limited number of patients to validate the already available study reports saying, uric acid can be used as a prognostic marker in heart failure.

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