

## ORIGINAL RESEARCH

# A Study of Correlation Between Uric Acid and Ejection Fraction in Heart Failure

Arun Kumar Tumuluri<sup>1</sup>, K N Sudha Ramana<sup>2</sup>

## ABSTRACT

**Introduction:** Left ventricular (LV) ejection fraction (EF) was known for a long time as a conventional predictor of heart failure (HF). In recent times it was observed that patients with chronic heart failure (CHF) often have raised levels of serum uric acid (SUA), resulting in the estimation that serum uric acid (SUA) could be involved in the prognosis of chronic heart failure (HF).

**Material and methods:** 30 patients above the age of 18 years, who were admitted in our hospital with symptoms and signs of Heart Failure were included in the study after being evaluated and confirmed by clinical, ECG and 2D echocardiography findings. Routine blood investigations were performed including uric acid analysis.

**Results:** Out of the 30 patients, 14(44%) were females and 16 (56%) were males. 11 patients had globalhypokinesia and 19 have regional wall motion abnormality (RWMA) as assessed by a two dimensional echocardiogram. The Uric acid range was highest at 8.5 -9.0mg/dl with 12 patients and lowest at 9.5 – 10 mg/dl with 3 patients. There is inverse correlation between serum uric acid levels with ejection fraction in patients with heart failure i.e. higher the uric acid levels lower the ejection fraction.

**Conclusion:** Our analysis also proves that serum uric acid levels are more in the severe functional disability patients(NYH III AND IV) implying that Uric acid levels can be used as a marker for cardiac dysfunction in heart failure patients in place of 2D ECHO

**Keywords:** Serum Uric Acid, Ejection Fraction, Heart failure

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## INTRODUCTION

Heart failure (HF)<sup>1</sup> is a clinical syndrome that occurs in pa-

tients who, because of an inherited or acquired abnormality of cardiac structure and or function, develop a constellation of clinical symptoms (dyspnea and fatigue) and signs (edema and rales) that lead to frequent hospitalizations, a poor quality of life, and a shortened life expectancy.<sup>1</sup>

In the United states of America, about 5.1 million people were estimated to have heart failure in 2009 according to WHO. 1 in every 9 deaths was estimated to be due to this.<sup>2</sup> Community-based studies indicate that 30–40% of patients die within 1 year of diagnosis and 60–70% within 5 years, mainly from worsening HF or as a sudden event.<sup>2</sup>

It is a known fact that gout and hyperuricaemia are associated with coronary heart disease, apart from other risk factors like hypertension, obesity, hypertriglyceridaemia, dyslipidaemias and diabetes mellitus.<sup>3-6</sup> The levels of uric acid rise within minutes during angioplasty and during coronary artery bypass operations.<sup>7</sup>

Uric acid is a product of xanthine metabolism. Elevated levels of xanthine oxidase causes conversion of hypoxanthine to xanthine and to uric acid which acts as an oxidative stress in heart failure.<sup>8</sup> This finding of excessive uric acid levels in chronic heart failure has lead to the recognition of association between heart failure and chronic inflammation thereby contributing to the oxidative damage to the myocardium.<sup>9,10</sup> Cell death, tissue hypoxia, and impaired metabolism in HF increase XO activity, leading to an overproduction of UA. Increased UA in the circulation of HF patients may result from an increased generation of UA, a decreased excretion of UA, or a combination of both; however, overproduction of UA appears to be the dominate factor accounting for elevated UA levels in CHF. Numerous studies have demonstrated the prognostic importance of hyperuricemia in patients with CHF. Anker et al. have reported that a high serum UA level is a strong, independent marker of poor prognosis in patients with moderate to severe CHF.<sup>11-14</sup>

We have therefore conducted this observational study to correlate the association between high uric acid levels with that of ejection fraction during heart failure.

## MATERIALS AND METHODS

This observational study is conducted in the Department of General Medicine in Mallareddy Medical College for Women andMahavir hospital and research centre, Hyderabad during the period of Two years. 30 patients above the age of 18 years, who were admitted into our hospital with symp-

toms and signs of Heart Failure were included in the study after being evaluated and confirmed by clinical, ECG and 2D echocardiography findings. Informed consent was taken from all the patients. Children and patients with other diseases like Gout, Chronic kidney disease, patients on hemodialysis, Chronic liver failure, patients on drugs like cyclosporine, pyrazinamide, ethambutol, levodopa. Immunosuppressed patients like Malignancy were excluded from the study.

Detailed inpatient data including age, sex, diabetes, hypertension and other coronary risk factors, previous history of heart failure were obtained from the patients. Blood samples were taken for Complete Blood Picture, Blood sugar, Blood urea and creatinine, Serum electrolytes, Uric acid, cardiac enzymes like CPK and CK-MB, Prothrombin time, Activated partial Thromboplastin time. Complete urine exam, Chest Xray, ECG, 2D echocardiography to assess the severity of the damage caused by various etiological factors for Heart Failure was done. The biochemical tests and hematological tests were done by standard techniques on autoanalysers.

Levels of uric acid were compared with LVEF (Left Ventricular Ejection Fraction) to assess its prognostic significance and also compared the serum uric acid levels with functional NYHA class.

**RESULTS**

Out of the 30 patients, 14(44%) were females and 16 (56%) were males (Fig :1)

The mean age group was 53.3 years, with the mean age group of females being 51.4 years and those of males being 55.3 years.

In the study group 13 were diabetics, 8 females and 5 males, 22 were hypertensive, 12 males and 10 females. 13 patients had CAD, 9 males and 4 females (Fig: 2).

Among the precipitating causes of Heart failure, 11 had DCM of which 7 male and 4 female patients and 19 patients had acute coronary syndrome (9 male and 10 female patients) Fig: 3). 11 patients had global hypokinesia and 19 have regional wall motion abnormality (RWMA) as assessed by a two dimensional echocardiogram

The Uric acid range was highest at 8.5 -9.0mg/dl with 12 patients and lowest at 9.5 – 10 mg/dl with 3 patients (table : 1) Ejection fraction range was 30 – 40 in 15 patients while only 6 patients had a range of 20 – 30 (table : 2)

There is inverse correlation between serum uric acid levels with ejection fraction in patients with heart failure i.e. higher the uric acid levels lower the ejection fraction (Fig: 4).

In our study, we observed a positive correlation between serum uric acid levels with NYHA class of patients with heart failure i.e. Patients with class III and Class IV have higher uric acid levels than class II and I.

Serum uric acid level was positive (7 mg / dl) in all 30 patients. All the patients have reduced left ventricular ejection fraction (LVEF < 50 %) and among 30 patients 11 have global hypokinesia and 19 have regional wall motion abnormality

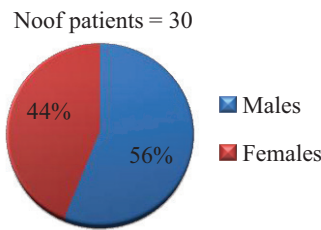


Figure-1: Gender wise distribution of patients.

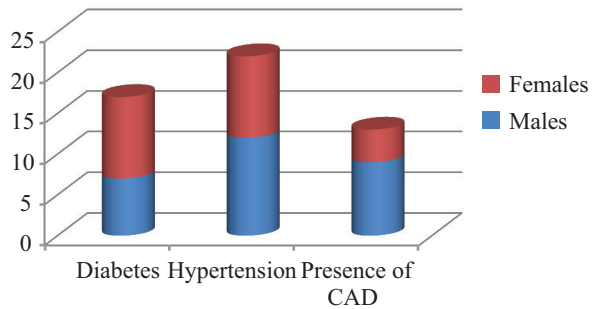


Figure-2: Presence of risk factors in patients

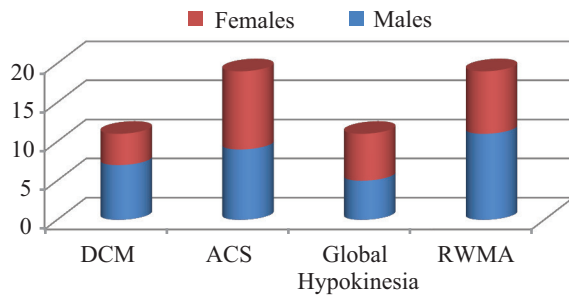


Figure-3: Precipitating causes of heart failure and results of 2D electrocardiogram

Value (mg/dl)	Number
8.0 – 8.5	10
8.5 – 9.0	12
9.0 – 9.5	5
9.5 – 10	3

Table-1: Uric acid range (mg/dl) analysis

Value	Number
20 – 30	6
30 – 40	15
40 - 50	9

Table-2: Ejection fraction range analysis

(RWMA) as assessed by a two dimensional echocardiogram

**DISCUSSION**

High levels of serum uric acid is a strong indicator of cardiovascular risk and poor prognosis. Though several explanations have been given for this association, the actual reasons for this mechanism is still unclear. Increased uric acid had been frequently found in patients with high blood pressure, diabetes, obesity and cardiovascular disease.

Our study showed an inverse correlation between serum uric

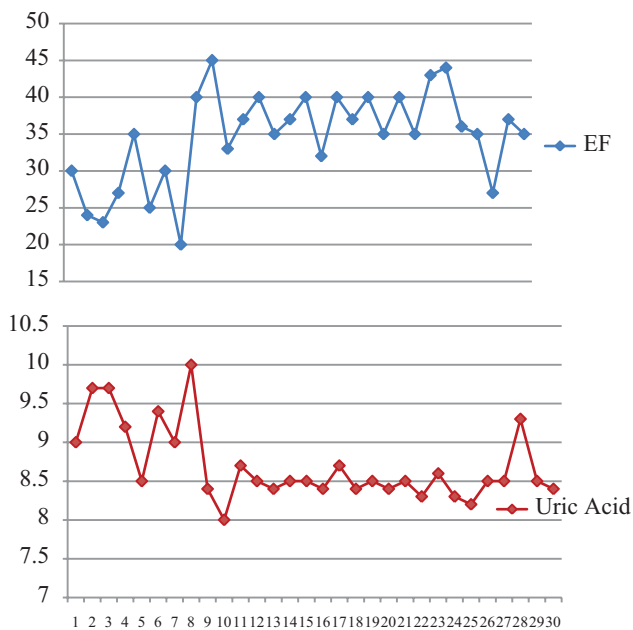


Figure-4: Correlation between serum uric acid and ejection factor

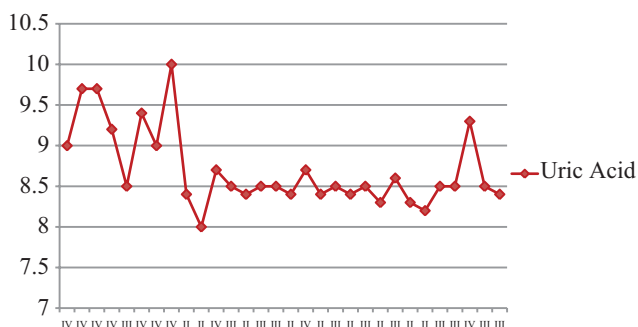


Figure-5: Correlation of Uric acid with NYHA class of patients

acid levels with ejection fraction in patients with heart failure i.e. higher the uric acid levels lower the ejection fraction. Similar results were observed by Pinelli et al who observed a negative relation between uric acid levels and ejection fraction showing that hyperuricaemia may be an indicator of deteriorating Cardiac Function.<sup>16</sup> In yet another study by XuDuan et al, the increase of serum UA level was found to be inversely associated with disease severity, cardiac function (LVEF) and prognosis of CHF, thereby corroborating our study.

Xanthine oxidase metabolic pathway as an important contributor to both symptoms of CHF as well as progression of the disease was observed by Doenher W et al in Germany.<sup>17</sup> In a study by Vaduganathan et al, it was reported that the mean uric acid levels was higher in males than that of females, though we have not observed such association. This also could be because of the fact that the sample size in our case were only fifty while that in the previous study was 3955.<sup>18</sup>

Our analysis also proves that serum uric acid levels are more in the severe functional disability patients(NYH III AND IV). Lower levels of uric acids were found in NYH II.

There have been recent studies on heart failure and it was ob-

served that apart from XO activity, Uric acid itself is found to play a role in the effect on heart failure. It was found that if uric acid levels were lowered, an improvement was observed in the cardiovascular outcome.<sup>19</sup> Another study reported that due to the inhibition of XO activity, an improvement in the efficiency of patients with CNF was observed.<sup>20</sup> Long-term high-dose allopurinol administration was associated with reduced mortality compared with long-term low-dose administration.<sup>21</sup> These studies show that XO inhibition seems to be a good strategy for the treatment of Heart failure. Also uric acid can be a better marker than 2D Echo for the detection of HF.

## CONCLUSION

Our analysis also proves that serum uric acid levels are more in the severe functional disability patients(NYH III AND IV). This implies that Uric acid levels can be used as a marker for cardiac dysfunction in heart failure patients in place of 2D ECHO.

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