



CORRELATION OF SERUM URIC ACID WITH SEVERITY OF HEART FAILURE

General Medicine

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ABSTRACT

OBJECTIVE: To evaluate serum uric acid levels in patients with heart failure and to study the relationship of serum uric acid level with left ventricular Ejection Fraction in patients of heart failure. **METHOD:** The study was a hospital based observational cross-sectional study conducted in MLN Medical College, Prayagraj, carried out over a period of 12 months from March 2019 to February 2020. 130 patients presenting with Heart Failure as diagnosed by Framingham Criteria of Heart Failure were included in this study. **RESULT:** Out of 130 subjects with heart failure 10 (7.7%) had preserved ejection fraction, 49 (37.7%) had mid-range EF and 71 (54.6%) reduced ejection fraction. Serum Uric acid level was increased in more than two-third (72.3%) of our study population. Mean serum uric acid of study subjects was 8.19 ± 2.56 mg/dl. Mean serum uric acid was significantly increased with severity of heart failure. In NYHA class I/II mean serum uric acid was 6.82 ± 1.80 and in NYHA class IV it was 10.37 ± 3.36 mg/dl. **CONCLUSION:** Moderate negative correlation was observed between Serum uric acid level and left ventricular ejection fraction which was found statistically significant (r value = -0.37; p value < 0.001).

KEYWORDS

Uric Acid, NYHA, LVEF, Framingham Criteria

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] HF affects an estimate of 26 million patients annually worldwide. This global incidence rate appears to remain stable over the years and this might be bound to increase as population gets older. Cardiovascular disease is responsible for 30% of all deaths in the world. In India cardiovascular diseases (CVD) have become the leading cause of mortality.^[2] Chronic heart failure (CHF) is a leading aetiology for both morbidity and mortality on a global level, resulting in an increase in both prevalence and health care costs. It carries a poor prognosis especially in the presence of concomitant diseases and confers a fivefold increase in the risk of sudden death.^[3] A number of biomarkers of severity of HF exist; brain natriuretic peptides, NT ProBNP, 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.^[4] Uric acid is the final product of purine metabolism in humans, and its level is determined by dietary intake, rate of cell turnover in the body and renal excretion. Uric acid appears to play a pathological role in the development of hypertension, diabetes, obesity and metabolic syndrome contributing to cardiovascular mortality. Elevated uric acid levels indicate cardiac dysfunction and progression of heart failure through oxidative stress and free radical injury by increased xanthine oxidase activity.^[5]

MATERIAL AND METHOD:

The study was a hospital based observational cross-sectional study conducted in MLN Medical College, Prayagraj, carried out over a period of 12 months from March 2019 to February 2020. Patients presenting with Heart Failure as diagnosed by Framingham Criteria of Heart Failure were included in this study.^[6] Patients of age group <18 Years, history of pre-existing Gout, chronic kidney disease, haematological malignancies and drug induced hyperuricemia [eg, Pyrazinamide, Ethambutol, Cyclosporine, (except diuretics) etc.] were excluded from the study.

Detailed history regarding risk factors, duration, symptoms, signs, aggravating factors of heart failure were taken. Questions were asked in relation to chest pain, dyspnoea, syncope, cough, smoking, medications and past history of myocardial infarction. A detailed physical examination was conducted to assess patients' volume status (rales, edema, jugular venous distension), weight, height, body mass index and blood pressure changes. Complete blood count, blood glucose (fasting and 2 hour post prandial), A1c, fasting serum lipid

profile, blood urea, serum creatinine and serum electrolytes were measured in all patients. ECG, Chest Xray, Echocardiography was performed in all patients. Serum samples for Uric acid measurements were collected within six hours of admission with reference range of 3.4 - 7.0 mg/dL in males and 2.4 - 5.7 mg/dL in females.

STATISTICAL ANALYSIS:

Total 130 subjects were included in the study. p value < 0.05 was taken as significant.

RESULT:

Mean age of study subjects was 56.23 ± 15.53 years with range of 18-96 years. Most of the participants were between the age group of 46-60 years (39.2%) followed by 61-75 years (32.3%) and 31-45 years (11.5%). Out of 130 subjects with heart failure, 74 (56.9%) were male while 56 (43.1%) were female. The male to female ratio was 1.32:1. 118 participants (90.8%) had dyspnoea, 102 (78.5%) had orthopnoea/PND and 84 (66.2%) had nocturnal cough. Other clinical features were hepatojugular reflex, elevated JVP, pedal oedema and hepatomegaly [Table 1]. Most common cause of heart failure in our study was coronary artery disease (40.0%) followed by Non ischemic DCMP/alcoholic/peripartum cardiomyopathy (39.2%), rheumatic heart disease (13.1%) and Chronic obstructive pulmonary disease (11.5%). Calcific AS/AR was responsible for 6.9% cases of heart failure. In our study subjects, hypertension was found in 75 (57.7%) participants, 61 (46.9%) were diabetics, and 49 (37.7%) were smoker. Dyslipidaemia was present in 56 (43.1%) subjects. Serum uric acid level was significantly higher in subjects with dyslipidaemia (8.93 ± 2.95 mg/dl) compare to those without dyslipidaemia (7.59 ± 2.34 mg/dl). This association was found statistically significant (p value = 0.01). History of alcohol intake was given by 31 (23.8%) study subjects. Out of 130 subjects with heart failure 10 (7.7%) had preserved ejection fraction, 49 (37.7%) had mid-range EF and 71 (54.6%) reduced ejection fraction. Serum Uric acid level was increased in more than two-third (72.3%) of our study population. Mean serum uric acid of study subjects was 8.19 ± 2.56 mg/dl.

Mean serum uric acid was significantly increased with severity of heart failure. In NYHA class I/II mean serum uric acid was 6.82 ± 1.80 , in NYHA class III mean serum uric acid was 8.38 ± 2.40 mg/dl and in NYHA class IV it was 10.37 ± 3.36 mg/dl. This association was statistically significant (p < 0.001) [Table 2]. There was significant rise of serum UA levels in patients with reduced ejection fraction. The mean UA levels of patients with LVEF of >50%, 40-49%, 30-39% and <30% were 6.10 ± 2.01 , 7.81 ± 2.64 , 8.32 ± 2.53 and 10.03 ± 2.72 mg/dL respectively [Table 3]. These results also show that serum uric acid

levels correlate negatively with ejection fraction in heart failure patients.

DISCUSSION:

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.^[7] In our study, serum uric acid level was significantly higher in severe heart failure patients with NYHA III and IV. Finding of our study were in concordance with Siddiki C et al^[8], in which 54.6% were NYHA III-IV in hyperuricemic patients, and 29.73% had serum uric acid levels greater than 8mg/dl. As the ejection fraction increased, the number of patients with elevated serum uric acid levels proportionately decreased (40% in patients with EF $\geq$ 50%). This association was statistically significant with a P value of <0.01 . There was significant rise of serum UA levels in patients with reduced ejection fraction. Study includes patients of Heart Failure on diuretics treatment so diuretics induced hyperuricemia can be a confounding factor in this study. Some patients were critically ill at the time of admission and expired after resuscitative efforts, so their serum uric acid level could not be measured and these patients were excluded from the study.

CONCLUSION:

Out of 130 subjects, 16 patients got expired during 1 month of follow-up so mortality was 12.3% in heart failure subjects. Serum uric acid level was significantly higher in subjects who expired during 1 month follow-up (9.92 ± 3.47 mg/dl) compared to those who survived (7.92 ± 2.48 mg/dl). Moderate negative correlation was observed between Serum uric acid level and left ventricular ejection fraction which was found statistically significant (r value = -0.37; p value <0.001). This study shows that elevated uric acid levels had negative correlation with ejection fraction proving that progressive hyperuricemia indicates cardiac dysfunction in heart failure. Study by Reddy SK et al^[9] also observed significant and inverse correlation observed between UA levels and LVEF (r=-0.81; p= <0.001).

Table 1: Clinical presentation in heart failure study subjects (n=130)

Clinical presentation	No.	%
Dyspnoea	118	90.8
Orthopnoea/PND	102	78.5
Hepatojugular reflex	100	76.9
Nocturnal cough	84	66.2
Elevated JVP (≥ 12 mm Hg)	76	58.5
Pedal oedema ($\geq 2+$)	66	50.8
Hepatomegaly	24	18.5
Weight loss ($>4-5$ kg) in 5 days in response to treatment	11	9.23

Table 2: Association of NYHA class with uric acid level (n=130)

NYHA class	Uric acid level (mg/dl)				P value
	Upto 7 mg/dl	7.1-8.0 mg/dl	8.1-9.0 mg/dl	>9.0 mg/dl	
Class I	3 (50.0%)	2 (33.3%)	1 (16.7%)	0 (0.0%)	<0.01
Class II	22 (53.7%)	10 (24.4%)	4 (9.8%)	5 (12.2%)	
Class III	11 (18.3%)	15 (25.0%)	10 (16.7%)	24 (40.0%)	
Class IV	4 (17.4%)	2 (8.7%)	4 (17.4%)	13 (56.5%)	
Total	40	29	19	42	

Table 3: Association of LVEF with uric acid level in heart failure subjects (n=130)

LVEF%	Uric acid level (mg/dl)				P value
	Upto 7 (n=40)	7.1-8.0 (n=29)	8.1-9.0 (n=19)	>9.0 (n=42)	
$<30\%$	1 (6.2%)	3 (18.8%)	2 (12.5%)	10 (62.5%)	<0.01
30-39%	14 (25.5%)	11 (20.0%)	10 (18.2%)	20 (36.4%)	
40-49%	19 (38.8%)	12 (24.5%)	7 (14.3%)	11 (22.4%)	
$\geq 50\%$	6 (60.0%)	3 (30.0%)	0 (0.0%)	1 (10.0%)	

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