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Association of Hyperuricemia Among Patients with Heart Failure

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A B S T R A C T

Objective: To determine the association of serum uric acid level with heart failure among patients presented at cardiology department of LUMHS.

Methodology: This descriptive, cross-sectional study was conducted in department of the cardiology from July - Nov 2024 at Liaquat University hospital Hyderabad. Patients with diagnosis heart failure, aged 20 to 60 years and both genders were included. Patients underwent echocardiography to assess the ejection fraction and a 5ml blood was taken from each patient to assess the serum uric acid level by hospital diagnostic laboratory. All the relevant data were recorded by study Performa, which were further entered and analyzed using SPSS version 24.

Results: Mean age of the patients was 51.12+11.37 years, with male predominance 64.8% and females were 35.2%. Out of all 80% patients had an ejection fraction (EF) <40% and 9.5% had an EF between 41-50%. Frequency of hyperuricemia was 57(54.3%). Pearson correlation coefficient showed negative correlation between ejection fraction and uric acid level. Furthermore, the hyperuricemia was significantly related to diabetes and overweight patients ($p<0.05$).

Conclusion: The hyperuricemia noted to be highly frequent among patients with heart failure and substantially related to the reduced ejection fraction, predominantly among diabetes and overweight patients.

Key words: Heart failure, Uric acid, EF, correlation

Introduction

The heart failure (HF) continues to be a most persistent challenges in modern cardiovascular medicine, according to current context affecting more than 56 million peoples throughout the world, with continuing to rising prevalence to ageing population and improved survival after ischaemic events.[1,2] Regardless of substantial advances in guideline-directed medical treatment, it is still related to the higher rates of hospitalization, recurrent decompensating, and the mortality, encouraging sustained interest in distinguishing inexpensive, extensively available biomarkers can enhance risk stratification and management guidence.[1,2]

Amongst the numerous comorbidities implicated in the progression of HF, raised uric acid level has concerned growing clinical and scientific consideration. Raised serum UA is a common finding across the spectrum of HF clinical profiles, and numerous cohort studies have determined that it independently predicts the adverse outcomes regardless of severity of disease or the renal function.[3,4] Among patients with mild-to-moderate chronic heart failure, raised UA has been shown to correlate with impaired exercise capacity, sensitive inflammatory activation, and raised risk of mortality, irrespective of New York Heart Association class.[3] Consequent analyses have further explained that this prognostic relationship among markedly increased among patients without concomitant chronic renal disease, reflecting that the raised UA in this

context replicates the pathogenic process rather than mildly renal excretion impairement.[4]

In terms of underlying mechanisms, the association between HF and the hyperuricemia is consideration to be mainly mediated through enhanced expression of xanthine oxidase, the terminal enzyme in the catabolism of purine, that generates reactive oxygen species along with UA.[5,6] Such oxidative burden is associated with endothelial dysfunction, myocardial fibrosis, contractility impairment, and inflammation of the vessels, thereby linking raised UA not only to severity of disease but potentially to the progression of disease itself.[5,6] Recent research studies continue to support these relationships in the populations of real-world. Among individuals with heart failure along with preserved ejection fraction, raised UA level has been revealed to independently predict both all-cause HF- associated hospitalization and mortality, with data reflecting that the reduction of UA over time may result in measurable prognostic benefits.[7] Correspondingly, modern observational cohorts from Chinese HFpEF populations and more comprehensive HF registries have established that the raised uric acid level is significantly related to short-term readmission and long-term adverse events.[8,9] In spite of this assembling evidence, substantial uncertainty perseveres regarding the precise prognostic threshold of the uric acid, its discrepancy impact across the HF features, and whether it characterizes a modifiable potential treatment target or simply a marker of underlying haemodynamic and the metabolic imbalance. Elucidating these associations are important to determining whether routine monitoring of uric acid should be carried out into risk evaluation and protocols of the management for patients with HF. Therefore, this study was aimed to determine the prevalence, clinical correlation and prognostic significance of the raised UA level among patients with HF.

Methodology

This descriptive**,** cross-sectional study was conducted in department of the cardiology from July - Nov 2024 at Liaquat University hospital Hyderabad. Duration of the study was six months after approval of synopsis. A sample calculation 0f 105 patients was done using the raosoft software for "Sample size calculation" by using the proportion (The prevalence of hyperuricemia was 54.7% in HF patients)[10] with 90% confidential interval and 8% of margin of error. Non probability consecutive sampling technique was used. All the cases aged ≥18 years of either gender, with confirmed diagnosis of HF (HFrEF, HFmrEF, or HFpEF) basis on current ESC/ACC/AHA criteria, with support of clinical presentation and findings of the echocardiography (LVEF), admitted with either acute decompensated heart failure or those attending outpatient (OPD) follow-up for chronic HF, with complete baseline clinical, laboratory, and echocardiographic information required for the study variables were included. Conversely the cases with history of implanted defibrillators and pacemakers, cases on urate lowering therapy, patients with end-stage renal failure or patients on hemodialysis, history of chronic liver diseases and steroid therapy, patients on thiazide diuretics therapy or having malignancy / on chemotherapy along with pregnant and lactating women and those who were not agreeing to take a part of study were excluded. A detailed medical history including family history, clinical examination including systolic and diastolic blood pressure and base line investigation was done. Informed consent was obtained from each case before enrolment in the study after explaining the purpose of study. Subsequently the patients underwent echocardiography to assess the ejection fraction. A 5ml blood was taken from each patient was send to Hospital laboratory to assess the serum uric acid level. All the expenses of blood tests were covered by the principal researcher. All the patients were monitored during the complete study period and data regarding demographic characteristics including uric acid level were recorded on Performa. Finally the data were entered and analyzed on SPSS version 26.0. Mean and standard deviation were used for quantitative variables, while frequency and percentage were used for categorical variables. Post stratification Chi-square test was applied taking p-value $\leq$0.05 as statistically significant.

Results

Overall 105 patients with HF were studied, with mean age of 51.12 ± 11.37 years, average disease duration of 32.66 ± 25.22 months, mean

systolic and diastolic BP were 113.61 ± 22.82 mmHg and 73.02 ± 15.12 mmHg, respectively, whereas mean BMI was 24.66 ± 2.49 kg/m². Males were in majority (64.8%), compared to females 35.2%. According to patients belonged to a poor socioeconomic status (68.6%). Rural areas residents were (55.2%) urban residents were (44.8%). Diabetic patients were 37.1% and family history of cardiovascular disease was noted in 14.3% of patients. Additionally, occupational status presented in table I.

Table I: Baseline and clinical characteristics of patients. (n=105)

Variable	Category	Statistics	
Age (years)		51.12 ± 11.37 years	
Duration of disease (months)		32.66±25.22 Months	
Systolic BP mmHg		113.61±22.82 mmHg	
Diastolic BP mmHg		73.02±15.12 mmHg	
BMI		24.66±2.49 kg/m²	
Gender	Male	68	64.8%
	Female	37	35.2%
Educational Status	Illiterate	56	53.3%
	Primary	34	32.4%
	Matric	12	11.4%
	Intermediate	02	01.9%
	Graduate	01	01.0%
Socioeconomic Status	Poor	72	68.6%
	Middle	33	31.4%
Residential Status	Rural	58	55.2%
	Urban	47	44.8%
Occupational Status	Jobless	08	07.6%
	Technician	05	04.8%
	Housewife	38	36.2%
	Labor	14	13.3%
	Shopkeeper	12	11.4%
	Teacher	09	08.6%
	Govt. servant	05	04.8%
	Driver	08	07.6%
	Computer operator	01	01.0%
	Waiter	01	01.0%
	Peon	04	03.8%
Diabetes Mellitus	Yes	39	37.1%
	No	66	62.9%
Family history CVD	Yes	15	14.3%
	No	90	85.7%

In all of the patients with heart failure, 80% had an ejection fraction (EF) of less than 40%, 9.5% had an EF between 41-50%, and 10.5% had an EF greater than 50%, as presented in figure 1.

According to the 57(54.3%) were diagnosed with Hyperuricemia, while the remaining 48 (45.7%) did not have hyperuricemia, as shown in figure 2.

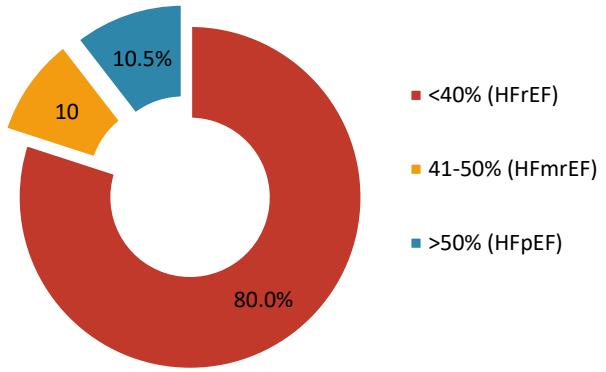

Figure: 1. Severity of EF among Patients with Heart Failure (n = 105)

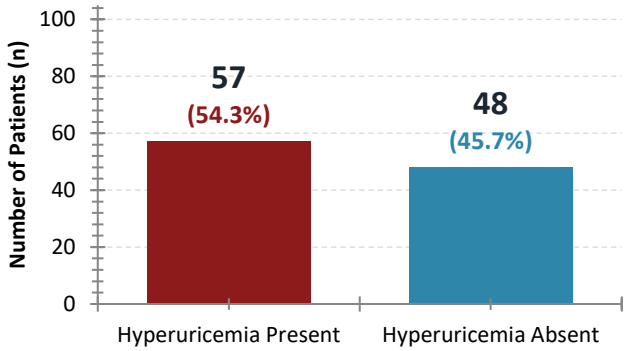

Figure 2. Frequency of Hyperuricemia in heart Failure patients (n = 105)

The hyperuricemia was significantly related to severity of EF (p=0.023), being EF <40% in 40 (38.1%) patients, EF 41–50% in 8 (7.6%) patients and EF >50% was in 9 (8.6%), out of a total of 57 (54.3%) patients with hyperuricemia among overall 105 patients. Table II.

Table II: Hyperuricemia according to severity of EF n=105

Variables		Hyperuricemia		Total	p-value
		Yes	No		
Ejection fraction	≤40%	40	44	84	0.023
		38.1%	41.9%	80.0%	
	41-50%	8	2	10	
		7.6%	1.9%	9.5%	
	>50%	9	2	11	
		8.6%	1.9%	10.5%	
Total		57	48	105	
		54.3%	45.7%	100.0%	

The Pearson correlation coefficient between ejection fraction and hyperuricemia was statistically significant p-value= 0.026. Figure 3.

The hyperuricemia was significantly linked to diabetes mellitus (DM) (p=0.0001) and BMI (p=0.001), being more common among DM

(31.4% versus 22.9%) and overweight cases (30.5%), while there was no significant association with gender SES residential status (p>0.05), as presented in table III.

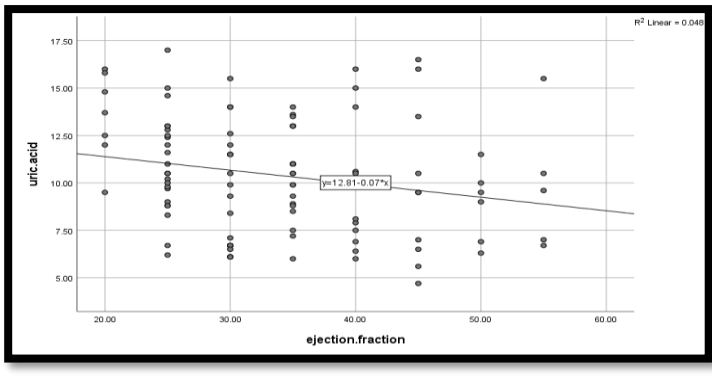

Figure 3. Correlation between EF and uric acid level n=105.

Table III: Frequency of Hyperuricemia according to gender n=105

Variables		Hyperuricemia		Total	p-value
		Yes	No		
Gender	Male	40	28	68	0.206
		38.1 %	26.7 %	64.8 %	
	Female	17	20	37	
		16.2 %	19.0 %	35.2 %	
Socioeconomic status	Poor	41	31	72	0.419
		39.0 %	29.5 %	68.6 %	
	Middle	16	17	33	
		15.2 %	16.2 %	31.4 %	
Residence	Rural	28	30	58	0.170
		26.7 %	28.6 %	55.2 %	
	Urban	29	18	47	
		27.6 %	17.1 %	44.8 %	
Diabetes mellitus	Yes	33	6	39	0.0001
		31.4 %	5.7%	37.1 %	
	No	24	42	66	
		22.9 %	40.0 %	62.9 %	
BMI (kg/m^2)	Normal	21	35	56	0.001
		20.0 %	33.3 %	53.3 %	
	Overweight	32	11	43	
		30.5 %	10.5 %	41.0 %	
	Obese	4	2	6	
		3.8%	1.9%	5.7%	

Discussion

HF is a chronic and progressive condition where the heart is unable to pump blood effectively to meet the requirement of body. The raised level of UA in the blood has been increasingly recognized as a common comorbidity among patients with HF. However, the association remains complex, involving various pathophysiological mechanisms, clinical implications, and therapeutic considerations. This study has been done on 105 cases with an overall mean age of 51.12 years to determine the association of serum uric acid level with heart failure with male predominance. In the comparison of this study Akçay FA et al[10] reported that the mean age of the study participants was 67.8 ± 13 years. Out of the 1,606 patients enrolled in for acute heart failure (AHF), 918 (57.2%) were men and 688 (42.8%) were women. Consistently Ud Din J et al[11] also reported that out of 100 patients, 60 were male and 40 were female, with an average age of 54 years. The male predominance across the studies may due to higher rates of smoking, use of alcohol and delayed preventive care, along with estrogen-related cardiovascular protection among women before menopause, as important factor to the observed gender disparity for risk of heart failure.

In the present study, hyperuricemia was observed in 54.3% of patients with heart failure, a figure that falls within the wide range reported across the literature and reaffirms uric acid as a common comorbid abnormality in this population, along with significant negative correlation with EF and more frequent among diabetes and overweight patients. The findings were in agreement with the study by Hamaguchi S et al[12] who consistently reported that among patients with heart failure, 56% were noted to have hyperuricemia based on definition as ≥7.0 mg/dL, along with cases with elevated uric acid levels (≥7.4 mg/dL) had higher rates of all-cause mortality, cardiac death, re-admission and the combined outcome of the readmission and death due to worsening HF. Our finding were also consistent with previous study by Palazzuoli A et al[13], where among 173 cases having HFrEF and 151 had HFpEF, the elevated UA level was more frequent in the HFpEF group (57% vs 43%), p=0.01, as well as also more frequent among females (74% vs 60%), in patients with diabetes

mellitus (39% vs 19%), hypertension (62% vs 43%) and atrial fibrillation (48% vs 34%), p=0.001. Additionally, in accordance with the findings of this study Carnicelli AP et al[14] the raided baseline serum UA level was in 68.9% of the cases, with elevated levels had a greater burden of comorbidities and poorer functional capacity on cardiopulmonary exercise testing compared to cases with normal levels of UA.

Moreover, a similar pattern was observed by Li L et al[15] where hyperuricemia was in 69.42% of patients overall in hospitalized patients with HF, along with similar prevalence across the age groups, genders, and BMI categories, though it varied by NYHA functional class and according to them based on multivariable analysis, hyperuricemia was independently linked to markers of renal dysfunction, hemodynamic impairment, electrolyte derangements and metabolic disturbance. Moreover consisting findings were also demonstrated by Liu X et al[8] who defined hyperuricemia as serum UA >7 mg/dL among males and >6 mg/dL among females with overall prevalence of around 57.6% among patients with HFpEF. However, the Rufe NB et al[16] reported that the in adult patients with CVD, the overall occurrence of hyperuricemia was around 41.3% and specifically was most frequent among those with congestive HF (48.0%), followed by cases with hypertensive heart disease (41.2%), which was slightly lower than this study. Though our findings were again supported by the Khan MU et al[17] where hyperuricemia being highly prevalent also around 59.29% among individuals with CHF, closely reflecting to our findings.

Furthermore, according to the severity of ejection fraction, this study showed a significant correlation between raised UA and reduced EF (p=0.023), with the majority of the cases with raised UA level falling in the EF <40% category, which was supported by above mentioned studies and also aligns with Jankowska et al[3] who reported an inverse correlation between serum UA level and LVEF (r=-0.31, p<0.01). The results were also comparable to those reported in the study by Wang et al[20] who stated that the raised UA level was an independent determinant of HFrEF (OR 1.247, 95% CI 1.172–1.328, p<0.001) according to a larger network-basis analysis. Overall, findings supported the concept that worsening systolic dysfunction is in conjunction with greater xanthine oxidase activation and oxidative stress, driving higher production of UA level as EF declines. Considering all above discussed findings, this stud largely consistent with international reported data, reinforcing that raised UA level among patients with HF is closely interlinked with falling ejection fraction and metabolic comorbidities like diabetes and obesity, rather than socioeconomic or demographic factors. How certain discrepancies in prevalence of hyperuricemia with few studies may be attributed to the variations in the used biochemical cut-off values to define hyperuricemia, along with differences in population, severity of disease and the dietary or regional factors. Hence, further larger network basis analysis are recommended specifically at local level incorporating standardized diagnostic criteria and additional relevant factors like severity of disease, duration of disease, regional and dietary factors, and other confounding influences to better define the true prevalence of hyperuricemia across diverse populations with HF.

Conclusion

The hyperuricemia was observed to be highly frequent among patients with heart failure and substantially related to decreased EF, diabetes mellitus, and overweight patients. Overall findings suggest serum uric acid may serve as a conventional, low-cost marker of metabolic and severity of cardiac disease, sustaining its potential role in the risk stratification. However, based on few substantial limitations, further longitudinal studies are recommended to validate the prognostic value and therapeutic implications.

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