


Original Research Paper

The correlation between hyperuricemia and the risk of congestive heart failure: a cross-sectional study in Indonesia**Farah Nadia¹, Sri Julyani^{2*} , Hanna Aulia Namirah³, Irna Diyana Kartika², Nurhikmawati Nurhikmawati⁴**¹Medical Education Study Program, Faculty of Medicine, Universitas Muslim Indonesia, Indonesia²Departement of Clinical Pathology, Faculty of Medicine, Universitas Muslim Indonesia, Indonesia³Departement of Ophthalmology, Faculty of Medicine, Universitas Muslim Indonesia, Indonesia⁴Departement of Cardiology, Faculty of Medicine, Universitas Muslim Indonesia, Indonesia sri.julyani@umi.ac.id

Submitted: January 17, 2024

Revised: March 15, 2025

Accepted: April 5, 2025

Abstract

Congestive Heart Failure (CHF) is a leading cause of morbidity and mortality worldwide and is the second most common cause of death in Indonesia. One factor that has recently gained attention is hyperuricemia, a condition characterized by elevated serum uric acid levels, which is closely linked to the pathogenesis of cardiovascular diseases. The underlying mechanism involves increased activity of the enzyme xanthine oxidase, which triggers oxidative stress, endothelial dysfunction, and systemic inflammation, all of which contribute to the progression of CHF. This study aims to examine the relationship between serum uric acid levels and the incidence of CHF at RSUD (Regional General Hospital) I Lagaligo, East Luwu Regency. This study employed observational analytic approach with cross-sectional design. Data were collected from the medical records of 102 CHF patients treated between January 2023 and June 2024. Uric acid levels and CHF types were classified based on ejection fraction (EF). Data analysis was done using the Chi-Square test. The results showed a significant association between uric acid levels and the type of CHF ($p < 0.001$). Among patients with reduced ejection fraction, 83.7% had elevated uric acid levels, while 55% of patients with preserved ejection fraction had normal levels. Conclusion: There is a significant correlation between uric acid levels and CHF. Monitoring uric acid levels has the potential to serve as a clinical indicator in the evaluation and management of CHF patients.

Keywords: congestive heart failure; uric acid**1. Introduction**

Heart failure is defined as a clinical syndrome characterized by signs and symptoms resulting from structural and/or functional abnormalities of the heart, accompanied by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion (PERKI, 2023). Globally, cardiovascular disease has been the leading cause of death for the past two decades. In Indonesia, congestive heart failure (CHF) is the second most common cause of death after stroke (Kementerian Kesehatan Republik Indonesia, 2020). According to the 2018 Basic Health Research (RISKESDAS) data, the prevalence of CHF diagnosed by physicians in Indonesia was 1.5%, or approximately 1,017,290 people. In South Sulawesi Province, the prevalence of heart disease was recorded at 1.46% (Kementerian Kesehatan Republik Indonesia, 2018).

Several factors contribute to the development of CHF, including age, sex, smoking, obesity, hypertension, and uric acid levels (Claire A. Lawson et al., 2020; Gong FF et al, 2018; Yang et al, 2016). Serum uric acid levels remain a widely studied and debated risk factor. Uric acid is the final product of purine metabolism. Hyperuricemia is a condition in which serum uric acid levels exceed normal thresholds, defined as more than 6.2 mg/dL in women and 7.0 mg/dL in men (Fiori et al., 2024).



Hyperuricemia in heart failure is associated with several mechanisms, including increased activity of xanthine oxidase (XO), an enzyme involved in uric acid synthesis, which is regulated by inflammatory cytokines and chemokines. Hyperuricemia is linked to vascular damage, endothelial dysfunction, and oxidative stress, all of which play critical roles in various stages of heart failure development and contribute to an increased risk of its onset (Berezin AE., 2017).

A study by Alshamari et al. (2022) found a significant association between serum uric acid levels and the incidence of CHF. However, a study by Pualilin et al. (2015) reported no such relationship.

Given these conflicting findings, the relationship between uric acid levels and the incidence of CHF remains a topic of debate. Therefore, this study aims to investigate the correlation between serum uric acid levels and the occurrence of CHF at *RSUD I Lagaligo*, East Luwu Regency.

2. Research Methods

This study employed observational analytic method with cross-sectional approach. It was conducted at *RSUD I Lagaligo*, located in Wotu District, East Luwu Regency, using medical records from January 2023 to June 2024. The study population consisted of patients diagnosed with congestive heart failure (CHF) at the hospital. The sample was selected using a total sampling technique, in which all members of the population who met the criteria were included. As a result, the sample size for this study was 102 patients who had recorded uric acid test results during the specified period. Inclusion criteria consisted of both inpatients and outpatients diagnosed with CHF at *RSUD I Lagaligo* during the study period and who had documented uric acid test results. Exclusion criteria included medical records with incomplete data. Data collection was based on secondary data obtained from patient medical records at *RSUD I Lagaligo*, Wotu District, East Luwu Regency that met the inclusion criteria. Data analysis was performed using SPSS software, with the Chi-Square test applied at a 95% confidence level to assess the relationship between uric acid levels and the incidence of CHF. Univariate analysis was used to describe the characteristics of each variable, while bivariate analysis was used to examine the relationship between two variables, specifically, the correlation between uric acid levels and the incidence of congestive heart failure.

This study adhered to ethical research principles by maintaining the confidentiality of patient medical records and ensuring that no parties were harmed by the research process. Ethical approval was obtained from Universitas Muslim Indonesia, with the approval number UMI012405292.

3. Results and Discussion

This study was conducted on 102 patients with congestive heart failure (CHF) who were treated at *RSUD I Lagaligo*, East Luwu Regency, from January 2023 to June 2024 and met the inclusion criteria.

Table 1. Characteristics of Congestive Heart Failure Patients

No	Characteristic	Frequency (n)	Percentage (%)
1	Age (years)		
	31-40	3	2.9
	41-50	12	11.8
	51-60	33	32.4
	61-70	35	34.3
	71-80	14	13.7
	81-90	5	4.9
2	Sex		
	Male	64	62.7
	Female	38	37.3

No	Characteristic	Frequency (n)	Percentage (%)
3	History of Hypertension		
	Yes	98	96.1
	No	4	3.9
4	History of Diabetes		
	Yes	20	19.6
	No	82	80.4
5	Kidney Function		
	Stage 1	10	9.8
	Stage 2	37	36.3
	Stage 3a	29	28.4
	Stage 3b	8	7.8
	Stage 4	11	10.8
	Stage 5	7	6.9
6	Smoking Habit		
	Smoker	67	65.7
	Non-smoker	35	34.3
	Total	102	100

Table 1 shows that the most frequent age group was 61–70 years, accounting for 35 patients (34.3%), while the least represented group was 31–40 years with only 3 patients (2.9%). By sex, the majority were male (64 patients or 62.7%), while females made up 38 patients (37.3%). Regarding hypertension, 98 patients (96.1%) had a history of hypertension, and 4 (3.9%) did not. For diabetes mellitus, 20 patients (19.6%) had a history of the disease, while 82 (80.4%) did not. In terms of kidney function, 37 patients (36.3%) had mild impairment, while 7 (6.9%) were diagnosed with kidney failure. As for smoking habits, 67 patients (65.7%) were smokers and 35 (34.3%) were non-smokers.

Table 2. Distribution of Congestive Heart Failure Types

CHF Type	Frequency (n)	Percentage (%)
HFrEF	43	42.2
HFmrEF	19	18.6
HFpEF	40	39.2
Total	102	100,0

Table 2 shows that most patients had heart failure with reduced ejection fraction (HFrEF), accounting for 43 individuals (42.2%), followed by those with preserved ejection fraction (HFpEF) at 40 (39.2%), and mildly reduced EF (HFmrEF) at 19 patients (18.6%).

Table 3. Serum Uric Acid Levels Among CHF Patients

			Uric Acid Status		Total
			Normal	Elevated	
CHF Type	HFrEF	n	7	36	43
		%	16.3%	83.7%	100.0%
	HFmrEF	n	5	14	19
		%	26.3%	73.7%	100.0%
	HFpEF	n	22	18	40
		%	55.0%	45.0%	100.0%
	Total		34	68	102

		Uric Acid Status		Total
		Normal	Elevated	
		33.3%	66.7%	100.0%
		%		

Table 3 shows that 36 patients (83.7%) with reduced ejection fraction (HFrEF) had elevated uric acid levels, while 7 patients (16.3%) had normal levels. In addition, 22 patients (55%) with preserved ejection fraction (HFpEF) had normal uric acid levels, while 18 patients (45%) had elevated levels.

Table 4. Cross-tabulation of CHF Type and Uric Acid Levels

			CHF Type			Total	p-value
			HFrEF	HFmrEF	HFpEF		
Uric Acid Status	Normal	n	7	5	22	34	<0.001
		%	20.6%	14.7%	64.7%	100%	
	Elevated	n	36	14	18	68	
		%	52.9%	20.6%	26.5%	100%	
Total	n		43	19	40	102	
	%		42.2%	18.6%	39.2%	100%	

Table 4 shows that the Chi-Square test yielded a p-value of <0.001, indicating a statistically significant relationship between serum uric acid levels and the type of CHF in patients treated at *RSUD* I Lagaligo, East Luwu Regency.

3.1.Characteristics of Congestive Heart Failure Patients

This study was conducted on 102 patients with congestive heart failure at *RSUD* I Lagaligo, East Luwu Regency, who met the inclusion criteria. Based on age group, the highest frequency was found in the 61–70 years group, with 35 patients (34.3%). This finding aligns with previous research conducted by Sherly et al. at *RSUP* (Central General Hospital) Dr. M. Djamil Padang, which reported 26 patients (45.6%) aged 60–74 years (Sherly et al., 2022), and by Donsu et al. at *RSUP* Prof. Dr. R. D. Kandou, where 49 patients (55%) were over 60 years old (Donsu et al., 2020).

This trend can be explained by age-related structural and functional changes in the heart, leading to a decline in left ventricular function. Blood vessels also lose elasticity, causing plaque accumulation and potentially blocking blood flow, which results in atherosclerosis that may progress to infarction and ultimately lead to heart failure (Li et al., 2020).

The distribution by sex showed that of the 102 patients, the majority were male (64 patients or 62.7%), while females accounted for 38 patients (37.3%). This is consistent with research by Donsu et al. (2020), which reported 52 male patients (58%) and 37 female patients (42%), and with Yulistia et al. (2020) at Haji General Hospital Medan, where 57 male patients (71.3%) and 23 female patients (28.8%) were reported (Donsu et al., 2020) (Nazlina Siregar & Septina, 2020). This pattern may be due to males generally having less healthy lifestyles, such as smoking and excessive alcohol consumption, which increase the risk of various diseases. In addition, females have estrogen, a hormone that protects against vascular damage and provides cardiovascular protection.

Based on history of hypertension, 98 patients (96.1%) had a history of hypertension, while only 4 (3.9%) did not. This supports the theory that hypertension is a major risk factor for heart failure. High blood pressure can cause significant cardiac damage. Excessive pressure makes blood vessels sclerotic, reducing blood and oxygen flow to the heart. The increased pressure and reduced blood flow can impair the heart's ability to pump, eventually leading to heart failure (Donsu et al., 2020).

Regarding history of diabetes mellitus, 82 patients (80.4%) had no history of diabetes, while 20 (19.6%) did. This finding is not consistent with a previous study by Komanduri et al. (2017), which reported an odds ratio of 2.06 (Saketram Komanduria et al., 2017). Heart failure can occur in patients with long-standing diabetes mellitus due to chronic high blood glucose levels, which thicken small blood vessels and impair oxygen and nutrient delivery. Thickened arterial walls can also lead to hypertension, further damaging the endothelium and contributing to heart failure (Nazlina Siregar & Septina, 2020). Diabetes also activates the RAAS pathway, which accelerates atherosclerosis, reduces cardiomyocyte numbers, and causes extensive myocardial fibrosis (Anak Agung Ketut Yunita Paramita et al., 2021). The difference in results may be because many patients in this study had comorbidities other than diabetes, with hypertension being the predominant cause of heart failure.

Renal function analysis showed that 90.2% of patients had decreased kidney function, ranging from mild impairment to kidney failure. This percentage is higher than reported in some previous studies. Adriyanti et al. (2017) found that 88.2% of heart failure patients had impaired renal function (Adriyanti et al., 2017).

This is consistent with the theory that reduced cardiac output leads to renal hypoperfusion, damaging glomerular interstitial tissue and impairing renal function. Reduced blood flow to the afferent arterioles triggers compensatory activation of the sympathetic nervous system, the renin-angiotensin-aldosterone system, and various peptides. These responses reduce glomerular filtration and kidney excretory function, resulting in the accumulation of waste in the body (Adriyanti et al., 2017).

Regarding smoking habits, 67 patients (65.7%) were smokers, while 35 (34.3%) were non-smokers. This supports existing theories that smoking raises blood pressure, total systemic vascular resistance, pulmonary artery pressure, and pulmonary vascular resistance, all known risk factors for heart failure (Ding et al., 2022). In addition, smoking increases exposure to carbon monoxide, which promotes oxidative stress, mitochondrial dysfunction, inflammation, endothelial dysfunction, and renal impairment, all of which contribute to the pathophysiology of heart failure (Kamimura et al., 2018).

3.2.Distribution of Congestive Heart Failure Patients

The distribution of congestive heart failure patients at *RSUD I Lagaligo* showed that out of 102 samples, the number of patients with reduced ejection fraction (Heart Failure with Reduced Ejection Fraction/HFrEF) was higher than those with preserved ejection fraction (Heart Failure with Preserved Ejection Fraction/HFpEF). A total of 42.2% patients had HFrEF, while 39.2% patients had HFpEF. These findings align with the 2021 guidelines of the European Society of Cardiology (ESC), which state that more than 50% of heart failure patients belong to the HFrEF group (McDonagh et al., 2021).

3.3.Distribution of Uric Acid Levels among Congestive Heart Failure Patients

Based on Table 3, patients with an ejection fraction value of <40% (HFrEF) had a higher proportion of elevated uric acid levels compared to those with ejection fractions >40%. These findings are consistent with a study conducted by Suresh et al. in 2016, which showed that heart failure patients with reduced ejection fraction (<40%) had worse uric acid profiles compared to those with preserved ejection fraction (>50%). This can occur because elevated uric acid levels lead to increased activity of reactive oxygen species (ROS), which stimulate Tumor Necrosis Factor-alpha (TNF- α). TNF- α binds to its receptor (TNF-R) in the heart, and continuous ROS stimulation can cause left ventricular hypertrophy and thickening of the heart muscle wall. This reduces blood supply to the heart and increases cardiac workload, ultimately impairing myocardial contractility and causing multi-organ dysfunction. This mechanism is particularly evident in patients with reduced ejection fraction (<40%) (Suresh et al., 2016).

3.4. The Relationship between Uric Acid Levels and the Incidence of Congestive Heart Failure

This study analyzed the relationship between uric acid levels and the incidence of congestive heart failure at *RSUD I Lagaligo*, East Luwu Regency. Statistical analysis using the Chi-Square test revealed a significant relationship, with a p-value of <0.001 , indicating a strong association between elevated uric acid levels and the incidence of congestive heart failure.

These results are in line with a study by Alshamari et al. (2022), which also found a significant association between uric acid levels and congestive heart failure, with a p-value of 0.039 (<0.05) (Alshamari et al., 2022). Similarly, research by Vlad-Sabin et al. (2021) showed that patients with higher uric acid levels had a greater risk of decreased ejection fraction compared to those with normal levels (Vlad-sabin et al., 2021).

Elevated uric acid levels have been linked to oxidative stress, endothelial dysfunction, inflammation, and cardiovascular events. Several studies have identified hyperuricemia as an independent prognostic factor associated with poor outcomes in heart failure patients (Shahin et al., 2021). Hyperuricemia appears to be a marker of altered oxidative metabolism, related to tissue hypoxia, which can damage cardiomyocytes and vascular endothelium. This can lead to impaired myocardial contractility, vasoconstriction, and a worsening cardiovascular profile, thereby potentially worsening the prognosis in heart failure patients (Vlad-sabin et al., 2021).

Treatment for HFpEF generally involves supportive care, weight loss (in obese patients), rehabilitation (exercise programs), identification and management of comorbidities, and pharmacological therapy. Non-dihydropyridine calcium channel blockers may be used for HFpEF. Loop diuretics are recommended for patients with HFrEF to relieve congestion, with furosemide being the currently available option in Indonesia (PERKI, 2023). Theoretical studies have shown that the use of calcium channel blockers is associated with a lower risk of hyperuricemia in hypertensive patients, while diuretics, beta-blockers, and ACE inhibitors are linked to increased risk (Rubio-Guerra et al., 2017).

According to the Indonesian Rheumatology Association's guidelines on the diagnosis and management of hyperuricemia and gout arthritis, foods such as red meat, organ meats, and processed meat products can increase serum uric acid levels and gout risk, and their consumption should be limited. Seafood, especially shrimp, lobster, crab, and shellfish, should also be restricted for the same reason. In addition, alcohol consumption, previous medication use, and lack of physical activity contribute to increased uric acid levels (Perhimpunan Reumatologi Indonesia, 2024).

4. Conclusion

Based on the results and discussion, it can be concluded that there is a significant relationship between elevated uric acid levels and the incidence of congestive heart failure, as indicated by a p-value of <0.001 . Patients with high uric acid levels were more likely to develop heart failure with reduced ejection fraction (HFrEF) compared to those with normal uric acid levels. A total of 83.7% of patients with HFrEF had elevated uric acid levels, while only 16.3% had normal levels. Conversely, patients with preserved ejection fraction (HFpEF) more commonly had normal uric acid levels (55%) than elevated levels (45%).

Further studies with larger sample sizes are recommended to further evaluate the impact of elevated uric acid levels on the incidence of congestive heart failure. Future research should also include multivariate analysis to explore other contributing factors that may influence the occurrence of congestive heart failure.

Acknowledgment

The researcher expresses her sincere gratitude to the academic supervisors for their guidance and input throughout the research process. Special thanks are also extended to RSUD I Lagaligo, Wotu Subdistrict, East Luwu Regency, for granting permission to conduct this study.

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