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INCIDENCE OF NEW-ONSET ATRIAL FIBRILLATION IN PATIENTS WITH AND WITHOUT HYPERURICEMIA

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ABSTRACT

Background: Hyperuricemia has been increasingly linked to cardiovascular diseases, yet its association with new-onset atrial fibrillation (AF) remains unclear.
Objective: To determine the incidence of new-onset atrial fibrillation in patients with and without hyperuricemia and assess whether hyperuricemia independently predicts AF development.
Methods: This prospective cohort study was conducted at Fauji Foundation Hospital, Lahore from 1st Oct 2024 to 5 April 2025. A total of 189 adult patients aged 18 years and above were enrolled in the study. Baseline demographic data including age, sex, body mass index (BMI), and comorbidities such as hypertension, diabetes mellitus, and smoking status were recorded. Laboratory tests including serum uric acid, creatinine, and lipid profile were documented at the time of enrollment.
Results: Out of the 189 patients, 94 (49.7%) had hyperuricemia. Atrial fibrillation developed in 19 patients (20.2%) in the hyperuricemia group and in 7 patients (7.4%) in the normouricemia group ($p = 0.01$). Kaplan-Meier analysis showed a significantly higher cumulative incidence of AF in the hyperuricemic group (log-rank $p = 0.008$). In multivariable Cox regression, hyperuricemia was independently associated with increased risk of new-onset AF (hazard ratio 2.73; 95% CI: 1.15–6.49; $p = 0.023$), along with age >65 years and hypertension.
Conclusion: It is concluded that hyperuricemia is significantly associated with an increased risk of new-onset atrial fibrillation. Serum uric acid may serve as a useful biomarker for AF risk stratification. Further studies are warranted to determine whether urate-lowering therapies could play a preventive role in atrial fibrillation development.

INTRODUCTION

About 33 million people worldwide have atrial fibrillation (AF) which is the most common lasting form of heart rhythm disorder and contributes to a lot of health problems and use of medical resources. Older individuals and those with hypertension, diabetes mellitus, obesity, chronic kidney disease (CKD) and coronary artery disease (CAD) are more likely to develop atrial fibrillation (AF) [1]. Apart from causing hemodynamic problems, AF raises the risk of stroke by five times and the risk of any death by two times. Because of these issues, it is vital to catch and address modifiable risk factors as early as possible in order to prevent heart disease. In the past, doctors mainly recognized serum uric acid (SUA) for causing gout and urate nephropathy [2]. There is now more discussion that hypertension plays a significant role in cardiovascular and metabolic diseases. Having SUA above 7 mg/dL for men and 6 mg/dL for women is considered more and more as not only a marker but also a cause of dysfunction in the blood vessels and heart [3]. Uric acid is thought to cause endothelial problems, increase oxidative stress, cause ongoing inflammation and start up the renin-angiotensin system all leading to changes in myocardium [4]. Data from several epidemiological studies indicate that having elevated SUA might lead to heart conditions such as hypertension, heart failure and ischemic heart disease [5]. Yet, exactly how hyperuricemia causes atrial fibrillation is not well understood, since the evidence so far is mixed. Certain cohort studies and meta-analyses show a link between increased uric acid and AF, but similar results after adjusting for heart disease risk factors come from others [6]. These differences in findings may be caused by the differences in study populations, the way hyperuricemia is defined, the durations of follow-up periods and the quality of the studies [7]. Further studies are needed to find out if hyperuricemia itself leads to AF or simply reflects a body state that supports tissue damage and arrhythmias [8]. Studies using experimental models support the idea that uric acid may promote atrial fibrosis by activating NLRP3 and transforming growth factor-beta (TGF-β) pathways [9]. The scarring in atrial tissue can cause defects in its electrical activity and encourage reentrant arrhythmias which may account for the link. Evidence also suggests that increased SUA may work together with insulin resistance and obesity which increases heart disease risk even more [10]. Since serum uric acid testing is both widely accessible and low-cost, it could possibly help identify who is likely to develop AF [11]. If researchers discover that hyperuricemia is linked with AF in new conditions, it may alert doctors to pay close attention to at-risk individuals which can promote active care or prevent serious consequences. Also, using drugs to reduce uric acid such as allopurinol or febuxostat, has been considered to see if it can help prevent AF, but conclusive evidence on this is still being worked out [12].

Objective

To determine the incidence of new-onset atrial fibrillation in patients with and without hyperuricemia and assess whether hyperuricemia independently predicts AF development.

Methodology

This prospective cohort study was conducted at Fauji Foundation Hospital, Lahore from 1st Oct 2024 to 5 April 2025. A total of 189 adult patients aged 18 years and above were enrolled in the study.

Inclusion Criteria

- Age ≥18 years
- Normal sinus rhythm at baseline ECG
- Available baseline serum uric acid values

- Willingness to participate and give informed consent

Exclusion Criteria

- History of prior atrial fibrillation or flutter
- History of structural heart disease (e.g., valvular heart disease, prior myocardial infarction with left ventricular dysfunction)
- Use of anti-arrhythmic drugs at baseline
- Renal failure requiring dialysis
- Ongoing malignancy or systemic inflammatory disease

Data collection

Patients were categorized into two groups based on their baseline serum uric acid levels:

- **Hyperuricemia group:** SUA >7.0 mg/dL in males or >6.0 mg/dL in females
- **Normouricemia group:** SUA within or below the above-defined thresholds

Baseline demographic data including age, sex, body mass index (BMI), and comorbidities such as hypertension, diabetes mellitus, and smoking status were recorded. Laboratory tests including serum uric acid, creatinine, and lipid profile were documented at the time of enrollment. All patients underwent a standard 12-lead ECG on recruitment and were monitored regularly during follow-up visits or in response to symptoms suggestive of arrhythmia, such as palpitations, syncope, or dizziness. The diagnosis of atrial fibrillation was confirmed by ECG, characterized by the absence of P-waves and the presence of an irregularly irregular ventricular response lasting more than 30 seconds. The primary outcome of the study was the incidence of new-onset atrial fibrillation in patients during the follow-up period.

Statistical Analysis

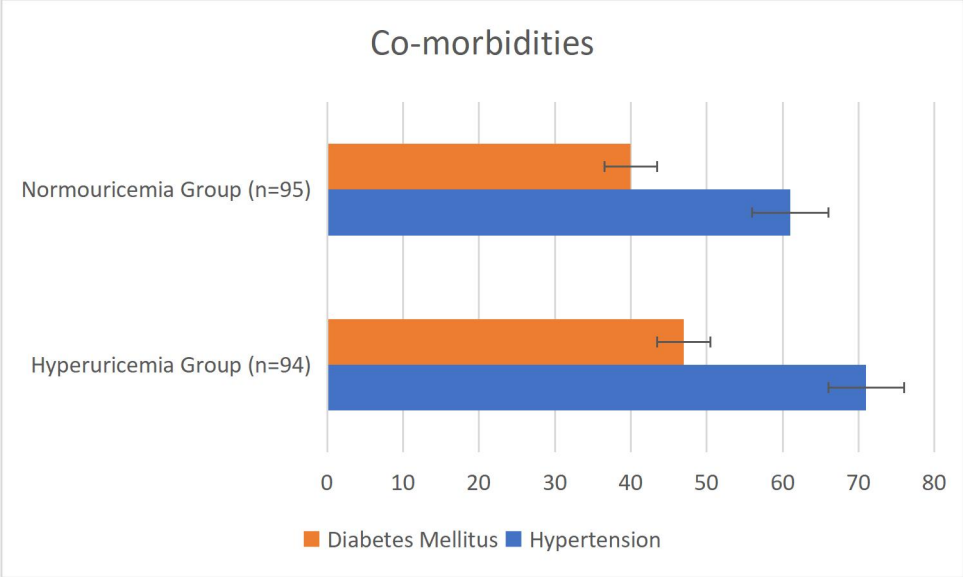
Data were analyzed using SPSS version 26. Continuous variables were expressed as means with standard deviations. Categorical variables were expressed as frequencies and percentages, with group differences assessed using the chi-square test. A p-value less than 0.05 was considered statistically significant.

Results

A total of 189 patients were added in the study, the mean age was slightly higher in the hyperuricemia group (62.1 ± 10.8 years) compared to the normouricemia group (60.3 ± 11.9 years), though this difference was not statistically significant ($p = 0.23$). The gender distribution was similar between the groups, with males comprising 59.6% of the hyperuricemia group and 56.8% of the normouricemia group ($p = 0.71$). Notably, the mean body mass index was significantly higher in the hyperuricemia group (28.4 ± 3.7 kg/m²) than in the normouricemia group (26.9 ± 3.2 kg/m²), with a p-value of 0.01. Additionally, hypertension was more prevalent in the hyperuricemia group (75.5%) compared to the normouricemia group (64.2%), and this difference reached statistical significance ($p = 0.04$). Although diabetes mellitus was more common in the hyperuricemia group (50.0% vs. 42.1%), the difference was not statistically significant ($p = 0.19$).

Table 1: Baseline Characteristics of the Study Population

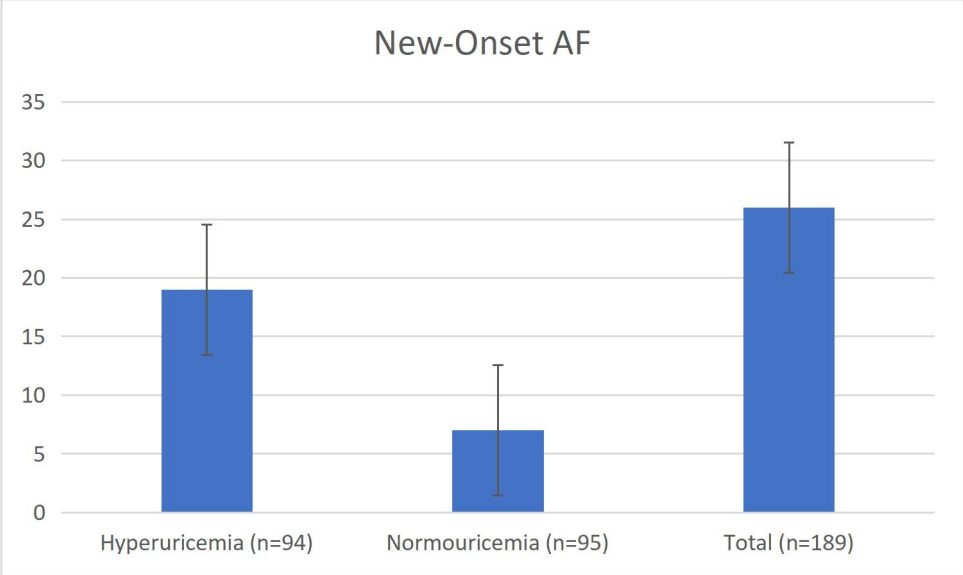
Variable	Hyperuricemia Group (n=94)	Normouricemia Group (n=95)	p-value
Age (years, mean ± SD)	62.1 ± 10.8	60.3 ± 11.9	0.23
Male Gender	56 (59.6%)	54 (56.8%)	0.71
BMI (kg/m², mean ± SD)	28.4 ± 3.7	26.9 ± 3.2	0.01
Hypertension	71 (75.5%)	61 (64.2%)	0.04
Diabetes Mellitus	47 (50.0%)	40 (42.1%)	0.19



New-onset atrial fibrillation occurred in 26 out of 189 patients (13.8%) during the follow-up period. The incidence was significantly higher in the hyperuricemia group, where 19 out of 94 patients (20.2%) developed atrial fibrillation, compared to only 7 out of 95 patients (7.4%) in the normouricemia group. This difference was statistically significant with a p-value of 0.01, indicating a strong association between elevated serum uric acid levels and increased risk of developing atrial fibrillation.

Table 2: Incidence of New-Onset Atrial Fibrillation

Group	New-Onset AF	p-value
Hyperuricemia (n=94)	19 (20.2%)	0.01
Normouricemia (n=95)	7 (7.4%)	
Total (n=189)	26 (13.8%)	



In multivariable Cox regression analysis, hyperuricemia was found to be a significant independent predictor of new-onset atrial fibrillation, with a hazard ratio of 2.73 (95% CI: 1.15–6.49; p = 0.023). Age greater than 65 years (HR: 1.89; 95% CI: 1.01–3.54; p = 0.045) and hypertension (HR: 2.04; 95% CI: 1.08–3.85; p = 0.029) were also significantly associated

with increased risk of atrial fibrillation. In contrast, diabetes mellitus (HR: 1.33; p = 0.37) and male gender (HR: 1.12; p = 0.71) did not show statistically significant associations in the adjusted model.

Table 3: Cox Regression Analysis for Predictors of New-Onset Atrial Fibrillation

Variable	Hazard Ratio (HR)	95% CI	p-value
Hyperuricemia	2.73	1.15–6.49	0.023
Age > 65 years	1.89	1.01–3.54	0.045
Hypertension	2.04	1.08–3.85	0.029
Diabetes Mellitus	1.33	0.71–2.49	0.37
Male Gender	1.12	0.61–2.04	0.71

Discussion

The scientists, through this cohort study, found that patients with hyperuricemia were more likely to have new-onset atrial fibrillation than those without hyperuricemia. In 189 patients followed for 12 weeks, those with elevated uric acid had atrial fibrillation 20.2 times more often than those with normal levels. They indicate that hyperuricemia is a risk factor for atrial fibrillation that may be preventable by lowering its level. Adjusting for age, hypertension, diabetes and renal function in a multivariable Cox regression analysis still produced a significant result [13]. A higher risk of atrial fibrillation was observed in people with hyperuricemia, proving that higher uric acid levels may be directly involved in heart remodeling and irregular conduction. Previous studies have suggested that uric acid could play a role in leading to arrhythmias which is also supported by these findings. In their study, Kuwabara et al. (2017) stated that SUA levels play a major role in triggering AF in a large Japanese population and similar findings have been seen in U.S. and European cohorts. There are possible explanations for how hyperuricemia can cause AF and these hypotheses are backed up by scientific studies more and more [14]. There is evidence that uric acid can boost oxidative stress, stimulate pro-inflammatory substances and disrupt the function of endothelium which adds to the structural and electrical changes in atrial tissues [15]. Uric acid may lead to atrial inflammation by activating the NLRP3 inflammasome and further fibrosis of the atria can happen because of TGF-β signaling which helps create an environment for heart arrhythmia. This might show why people with high uric acid have an increased risk of atrial fibrillation, even if they do not have heart disease [16]. It was also noted that people with hypertension and advanced age were more likely to have atrial fibrillation, as research [17] has pointed out. Still, other aspects like being male and having diabetes mellitus did not have significant effects which could be related to having few participants or other overlapping health problems [18]. Our research shows that adding serum uric acid gives more useful information for assessing the risk of atrial fibrillation. Since this type of testing is both affordable and accessible, using it in routine heart screenings could quickly discover who faces a greater risk for heart problems [19,20]. Raising the question of why gout often develops prior to AF, this finding suggests that drugs used to lower uric acid such as allopurinol and febuxostat, may be able to reduce the risk of AF in at-risk patients and should be studied in clinical trials. The study is strong because it was prospective, included people who fit specific criteria and relied on ECG for AF diagnosis. But there are some restrictions we should keep in mind. The follow-up observation time is short, so it might not pick up infrequent, progressive forms of AF. Even after considering the main confounders, there might be some impact from variables such as alcohol use, sleep apnea or left atrial volume, since these were not considered.

Conclusion

It is concluded that hyperuricemia is significantly associated with an increased incidence of new-onset atrial fibrillation, independent of other established cardiovascular risk factors such as age, hypertension, and diabetes mellitus. Patients with elevated serum uric acid levels demonstrated a markedly higher risk of developing atrial fibrillation compared to those with normal levels. These findings suggest that serum uric acid may serve not only as a marker of metabolic dysfunction but also as a potential contributor to atrial arrhythmogenesis. Routine monitoring of uric acid levels may aid in the early identification of individuals at elevated risk for atrial fibrillation, and future studies should explore whether urate-lowering interventions can modify this risk and improve cardiovascular outcomes.

References

1. Xiong J, Shao W, Yu P, Ma J, Liu M, Huang S, Liu X, Mei K. Hyperuricemia Is Associated With the Risk of Atrial Fibrillation Independent of Sex: A Dose-Response Meta-Analysis. Front Cardiovasc Med. 2022 Apr 7;9:865036. doi: 10.3389/fcvm.2022.865036. PMID: 35463784; PMCID: PMC9021846.
2. Cui H, Nie H, Wang C, Zhang N, Wang Y, Liu W, Huang S, Chen X, Jia H, Shu S, Fu M, Zhao Q, Hua X, Chang Y, Song Y, Song J. Phenotype-Based Classification of Obstructive Hypertrophic Cardiomyopathy Undergoing Myectomy. JACC Basic Transl Sci. 2025;10(5):568–83. doi:10.1016/j.jacbts.2024.12.016.
3. *Kirça M, Oguz N, Çetin A, Uzuner F, Yeşilkaya A. Uric acid stimulates proliferative pathways in vascular smooth muscle cells through the activation of p38 MAPK, p44/42 MAPK and PDGFRβ. J Recept Signal Transduct Res. (2017) 37:167–73. 10.1080/10799893.2016.1203941*
4. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and coronary heart disease: a systematic review and meta-analysis. Arthritis Care Res (Hoboken). 2010;62(2):170–80.
5. Richette P, Perez-Ruiz F, Doherty M, Jansen TL, Nuki G, Pascual E, et al. Improving cardiovascular and renal outcomes in gout: what should we target? Nat Rev Rheumatol. 2014;10(11):654–61.
6. Selvaraj S, Claggett BL, Pfeffer MA, Desai AS, McCausland FR, McGrath MM, et al. Serum uric acid, influence of sacubitril-valsartan, and cardiovascular outcomes in heart failure with preserved ejection fraction: PARAGON-HF. Eur J Heart Fail. 2020;22(12):2093–101.
7. Ali N, Perveen R, Rahman S, Mahmood S, Rahman S, Islam S, et al. Prevalence of hyperuricemia and the relationship between serum uric acid and obesity: a study on Bangladeshi adults. PLoS One. 2018;13(11):e0206850.
8. Haque T, Rahman S, Islam S, Molla NH, Ali N. Assessment of the relationship between serum uric acid and glucose levels in healthy, prediabetic and diabetic individuals. Diabetol Metab Syndr. 2019;11:49.
9. Ali N, Miah R, Hasan M, Barman Z, Mou AD, Hafsa JM, et al. Association between serum uric acid and metabolic syndrome: a cross-sectional study in Bangladeshi adults. Sci Rep. 2020;10(1):7841.
10. Molla NH, Kathak RR, Sumon AH, Barman Z, Mou AD, Hasan A, et al. Assessment of the relationship between serum uric acid levels and liver enzymes activity in Bangladeshi adults. Sci Rep. 2021;11(1):20114.
11. Kuma A, Mafune K, Uchino B, Ochiai Y, Enta K, Kato A. Development of chronic kidney disease influenced by serum urate and body mass index based on young-to-middle-aged Japanese men: a propensity score-matched cohort study. BMJ Open. 2022;12(1):e049540.

12. Li S, Cheng J, Cui L, Gurol ME, Bhatt DL, Fonarow GC, et al. Cohort study of repeated measurements of serum urate and risk of incident atrial fibrillation. J Am Heart Assoc. 2019;8(12):e012020.
13. Kuwabara M, Niwa K, Nishihara S, Nishi Y, Takahashi O, Kario K, et al. Hyperuricemia is an independent competing risk factor for atrial fibrillation. Int J Cardiol. 2017;231:137–42.
14. Mantovani A, Rigolon R, Civettini A, Bolzan B, Morani G, Bonapace S, et al. Hyperuricemia is associated with an increased prevalence of paroxysmal atrial fibrillation in patients with type 2 diabetes referred for clinically indicated 24-h Holter monitoring. J Endocrinol Invest. 2018;41(2):223–31.
15. Liu T, Zhang X, Korantzopoulos P, Wang S, Li G. Uric acid levels and atrial fibrillation in hypertensive patients. Intern Med. 2011;50(8):799–803.
16. Tamariz L, Hernandez F, Bush A, Palacio A, Hare JM. Association between serum uric acid and atrial fibrillation: a systematic review and meta-analysis. Heart Rhythm. 2014;11(7):1102–8.
17. Zhang CH, Huang DS, Shen D, Zhang LW, Ma YJ, Wang YM, et al. Association between serum uric acid levels and atrial fibrillation risk. Cell Physiol Biochem. 2016;38(4):1589–95.
18. Zhang J, Zheng R, Li H, Guo J. Serum uric acid and incident atrial fibrillation: a systematic review and dose-response meta-analysis. Clin Exp Pharmacol Physiol. 2020;47(11):1774–82.
19. Sun GZ, Guo L, Wang J, Ye N, Wang XZ, Sun YX. Association between hyperuricemia and atrial fibrillation in rural China: a cross-sectional study. BMC Cardiovasc Disord. 2015;15:98.
20. Chen Y, Xia Y, Han X, Yang Y, Yin X, Qiu J, et al. Association between serum uric acid and atrial fibrillation: a cross-sectional community-based study in China. BMJ Open. 2017;7(11):e019037.