BMC Pulmonary Medicine

RESEARCH

Open Access

The importance of uric acid levels in geriatric patients with respiratory failure under noninvasive mechanical ventilation in the respiratory intensive care unit

Murat Yıldız[1*], Deniz Çelik[2], Tarkan Özdemir[1], Güler Eraslan Doğanay[3], Melek Doğanci[3], Mustafa Özgür Cırık[3], Maşide Arı[1], Kerem Ensarioğlu[1], Ayşe Cifci[4] and Derya Kızılgöz[1]

Abstract

Introduction The respiratory system is critical for gas exchange, with respiratory failure resulting in insufficient oxygen and inadequate removal of carbon dioxide. Serum uric acid (SUA), a byproduct of purine metabolism, rises during hypoxemic conditions and has potential as a prognostic marker in respiratory failure. This study aimed to explore the relationship between SUA levels, mortality, duration of hospital stay, and ICU scores (APACHE II, and SOFA) in geriatric patients receiving non-invasive mechanical ventilation (NIV).

Materials and methods We conducted a retrospective analysis of 1109 patients with respiratory failure admitted to the Respiratory Intensive Care Unit (RICU) from 2020 to 2022. We excluded minor patients (under 18 years old), patients with incomplete records, known gout, and dialysis-dependent or SRRT required renal failure. We collected demographics, comorbidities, laboratory findings, APACHE II, and SOFA scores. Patients were divided into two age groups (≥ 65 and < 65). Statistical analysis, including chi-square, regression, and correlation tests, was performed to evaluate the association between SUA and clinical outcomes.

Results Patients aged ≥ 65 had significantly higher SUA, creatinine, and BUN levels, as well as longer hospital stays and higher APACHE II and SOFA scores. Elevated SUA levels correlated with increased mortality and NIV requirements in the elderly. Regression analysis confirmed SUA as a predictor of NIV need.

Discussion SUA levels are positively associated with worse outcomes in elderly patients with respiratory failure. This study supports previous research findings that hyperuricemia correlates with increased ICU admissions and mortality in respiratory conditions, particularly in older adults who need a noninvasive ventilation (NIV).

Conclusion Elevated SUA levels are a valuable prognostic marker for predicting NIV needs and poor outcomes in geriatric patients with respiratory failure. Regular monitoring of SUA could enhance clinical management and improve prognosis in this population.

*Correspondence:
Murat Yıldız
drmuratyildiz85@gmail.com

Full list of author information is available at the end of the article

Keywords Respiratory failure, Serum uric acid, Non-invasive mechanical ventilation, Geriatric patients, ICU scoring systems, Mortality prediction

Introduction

Respiratory failure, characterized by inadequate gas exchange leading to hypoxemia or hypercapnia, remains a critical concern in intensive care units (ICUs). Type 1 respiratory failure is primarily due to impaired oxygenation, while type 2 respiratory failure results from ineffective carbon dioxide elimination. Both conditions lead to metabolic complications, such as increased anaerobic metabolism and ATP degradation, which eventually cause elevated serum uric acid (SUA) levels [1].

Recent studies suggest that SUA may serve as a prognostic biomarker for critically ill patients, particularly those with respiratory failure. Uric acid, a product of purine metabolism, exhibits dual properties as both an antioxidant and a pro-oxidant, depending on the metabolic state [2]. As a result of hyperuricemia, oxidative stress and systemic inflammation increase. These two important processes are linked to the development of acute respiratory distress syndrome (ARDS) and multiorgan dysfunction syndrome (MODS). Additionally, elevated uric acid levels impair endothelial function and reduce nitric oxide synthesis, leading to an increase in pulmonary vascular resistance. Watanabe et al. have reported that hyperuricemia inhibits vasodilation in the pulmonary arteries and may contribute to the development of pulmonary hypertension [3].

Scoring systems like the Sequential Organ Failure Assessment (SOFA) and the Acute Physiology and Chronic Health Evaluation (APACHE) have been used for a long time in intensive care units to predict respiratory failure outcomes. However, metabolic biomarkers like SUA are gaining more interest for their potential to improve early prognosis and risk stratification [4]. In a recent study, suggesting a strong correlation between hyperuricemia and poor clinical outcomes, patients with increased SUA levels suggested higher ICU mortality rates and an increased risk of acute kidney injury (AKI) [5]. Despite these associations, the role of SUA in respiratory failure prognosis is still under investigation. Certain research indicates that SUA alone may not be sufficient to predict mortality in sepsis-related respiratory failure [2]. However, SUA may provide valuable insights into disease severity and patient survival rates when combined with other markers, such as the blood urea nitrogen-to-albumin ratio (BAR) [6].

Further research is necessary to establish SUA as a reliable biomarker for ICU patients with respiratory failure, given its ease of measurement and affordability. Our study aims to investigate the correlation between SUA levels and clinical outcomes in geriatric patients receiving non-invasive mechanical ventilation due to respiratory failure. These clinical outcomes include mortality, length of hospital stay, and ICU severity scores. By identifying metabolic markers that predict disease progression, we hope to enhance early intervention strategies and optimize patient management in ICUs.

Materials and methods

The Clinical Research Ethics Committee of the XXXXXX Training and Research Hospital approved this study on 27.09.2023, with Decision No: 2012-KAEK-15/2790. A total of 1378 patients, admitted and monitored in the Respiratory Intensive Care Unit between 01/01/2020 and 31/12/2022, were screened. 1109 patients with respiratory failure who met the study's criteria were included. We excluded patients younger than 18 years old, those whose medical records were missing, or those who had gout disease, dialysis-dependent renal failure, or a kidney transplant. Our study was conducted in a secondary-level respiratory intensive care unit, which is a specialized ICU primarily dedicated to the management of patients with type 1 and type 2 respiratory failure. In this unit, although the etiologies vary, patients with decompensated respiratory acidosis or hypoxemic patients with a low PaO_2/FiO_2 ratio and high oxygen demand are admitted and monitored.

All data, including age, gender, comorbidities, laboratory findings, Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA) scores, and demographic and clinical data were obtained from patient files and the hospital information management system. The diagnosis of "respiratory failure" was confirmed based on arterial blood gas (ABG) values during admission and follow-up. The patients were divided into two groups: those aged 65 years and older and those younger than 65 years. Retrospective analysis was performed on the blood parameters routinely monitored during intensive care follow-up. These blood parameters were compared between the two groups, and their effects on mortality and hospital length of stay were examined.

Statistical evaluation

Initially, a Microsoft Excel Office 365 file contained all study parameters for evaluation. After investigation for any mistakes, the file was then converted, and the following statistical evaluations were performed in an IBM SPSS Statistics file (IBM Corp. Released 2017; IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY).

We evaluated the parameters' distribution using a histogram and a Q-Q plot analysis to confirm the parametric distribution. We then presented the values by stating the mean and standard deviation. The Chi-square test was used to evaluate the association with two nominal parameters, with Phi and Cramer's V being used for parameters with more than two nominal values. Kendall's tau b was used to compare outcome parameters to other continuous parameters, in which discharge was assumed as the best outcome, with exitus considered the worst outcome. The role of each parameter on non-invasive mechanical ventilation (NIV) was investigated by binominal regression analysis. While linear regression analysis was planned for the impact of each parameter on intensive care unit (ICU) scoring parameters. A p-value of or below 0.05 was accepted as statistically significant.

Results

A total of 1378 patients' records were evaluated. After the exclusion criteria of 1378 and 269, the remaining 1109 patients were included in the study. The majority of the patients were older than 65 years ($n = 756$), and the average age was 75.61 (± 6.99) years. Both groups were predominantly male (62.4%, $n = 692$). The average intensive care duration for patients was 8.38 (± 5.26), which was higher in the elderly group (8.64 to 7.84, $p = 0.001$). Type-two respiratory failure was the dominant respiratory pattern in both age groups (Table 1).

Table 1 Demographic parameters and comorbidities of patients according to age

Parameters		Below 65 Years ($n = 353$) (n,%)	Above 65 Years ($n = 756$) (n,%)	Total ($n = 1109$) (n,%)	*p*-value
Age*(years, SD)*		56.56 (± 6.64)	75.61 (± 6.99)	69.61 (± 11.21)	
Hospitalization Duration*(Days, ±SD)*		7.84 (± 4.60)	8.64 (± 5.53)	8.38 (± 5.26)	**0.001**
Gender	*Male*	255 (72.24)	437 (57.8)	692 (62.4)	**0.001**
	Female	98 (27.76)	319 (42.2)	417 (37.6)	
Respiratory Failure Type	*Type 1*	73 (20.74)	174 (23.11)	247 (22.4)	0.378
	Type 2	279 (79.26)	579 (76.89)	858 (77.6)	
Chronic Obstructive Pulmonary Disease	*Not Present*	119 (33.71)	252 (33.33)	371 (33.5)	0.901
	Present	234 (66.29)	504 (66.67)	738 (66.5)	
Pneumonia	*Not Present*	310 (87.82)	599 (79.23)	909 (82)	**0.001**
	Present	43 (12.18)	157 (20.77)	200 (18)	
Diabetes Mellitus	*Not Present*	337 (95.47)	709 (93.78)	1046 (94.3)	0.259
	Present	16 (4.53)	47 (6.22)	63 (5.7)	
Interstitial Lung Disease	*Not Present*	339 (96.03)	717 (94.84)	1056 (95.2)	0.386
	Present	14 (3.97)	39 (5.16)	53 (4.8)	
Lung Malignancy	*Not Present*	329 (93.2)	728 (96.3)	1057 (95.3)	**0.023**
	Present	24 (6.8)	28 (3.7)	52 (4.7)	
Pulmonary Thromboembolism	*Not Present*	339 (96.03)	725 (95.9)	1064 (95.9)	0.916
	Present	14 (3.97)	31 (4.1)	45 (4.1)	
Congestive Heart Failure	*Not Present*	347 (98.3)	722 (95.5)	1069 (96.4)	**0.020**
	Present	6 (1.7)	34 (4.5)	40 (3.6)	
Atrial Fibrillation	*Not Present*	343 (97.17)	735 (97.22)	1078 (97.2)	0.959
	Present	10 (2.83)	21 (2.78)	31 (2.8)	
Bronchiectasis	*Not Present*	343 (97.17)	747 (98.81)	1090 (98.3)	**0.05**
	Present	10 (2.83)	9 (1.19)	19 (1.7)	
Acute Renal Failure*	*Not Present*	349 (98.87)	732 (96.83)	1081 (97.5)	**N/A**
	Present	4 (1.13)	24 (3.17)	28 (2.5)	
Chronic Renal Disease	*Not Present*	350 (99.15)	751 (99.34)	1101 (99.3)	**N/A**
	Present	3 (0.85)	5 (0.66)	8 (0.7)	
Obstructive Sleep Apnea	*Not Present*	349 (98.87)	751 (99.34)	1100 (99.2)	**N/A**
	Present	4 (1.13)	5 (0.66)	9 (0.8)	
Kyphoscoliosis	*Not Present*	346 (98.02)	755 (99.87)	1101 (99.3)	**N/A**
	Present	7 (1.98)	1 (0.13)	8 (0.7)	
Coronary Arterial Disease	*Not Present*	352 (99.72)	751 (99.34)	1103 (99.5)	**N/A**
	Present	1 (0.28)	5 (0.66)	6 (0.5)	

SD: Standard Derivation, For independent samples, a t-test was used to compare hospitalization duration, while Pearson chi-square was used for categorical data. Data with inadequate samples for chi-square analyses were removed and labeled as N/A. The diabetes mellitus definition included type 1 and type 2 diabetes yet excluded treatment-related diabetes

* These patients did not have dialysis-dependent or SRRT-required renal failure

The most prevalent comorbidity was chronic obstructive pulmonary disease, seen at 66.5% ($n=738$) of the study group, and did not vary between groups. This was followed by diabetes mellitus ($n=63$), interstitial lung disease ($n=53$), lung malignancy ($n=52$), pulmonary thromboembolism ($n=45$), congestive heart failure ($n=40$), atrial fibrillation ($n=31$), and bronchiectasis ($n=19$). Out of these, lung malignancy and congestive heart failure differed between groups. These two comorbidities were more common in the elderly group ($p=0.023$ and 0.020, respectively) (Table 1).

Regarding laboratory levels comparison, the elderly population had an overall higher uric acid, creatinine, blood urea nitrogen, sodium, and calcium levels ($p=0.001$ for all values). Similarly, the elderly group had a higher APACHE II and SOFA score ($p=0.001$ for both values). There was a difference in outcomes between elderly and non-elderly patients after ICU. Elderly patients required more frequent admissions to a ward (14.4–11.6%) or to another ICU for follow-up care (13.5–7.6%). They also had a lower overall discharge rate and a higher rate of intensive care mortality (63.9–74.2% and 8.2–6.5%). However, this association had a small magnitude of effect ($p=0.004$ and a Cramer V of 0.109) (Table 2).

We performed correlation analysis for parameters affecting ICU scoring systems, NIV requirements, and outcome evaluation. Uric acid levels positively correlated with an increased SOFA score in patients below 65 years old ($p=0.006$, correlation coefficient = 0.149). There was a stronger correlation coefficient (0.266) in the older population. There was also a positive correlation between uric acid, APACHE II score, and NIV requirement ($p=0.001$ for both values and correlation coefficients 0.164 and 0.125) (Tables 3 and 4).

Binominal regression analysis was performed to determine the role of the correlated parameters in NIV requirements. As patients below 65 years old did not correlate with uric acid and NIV requirements, the analysis was performed for those above 65 years old. The regression model was statistically significant ($\chi^{2(13)}=402.014$, $p=0.001$) and explained 62.5% (Nagelkerke R^2) of the variance. The Hosmer and Lemeshow test result was 0.305, which favored a good fit. The model correctly classified 84.4% of the patients. In the regression model, uric acid levels were still statistically significant in their role upon NIV requirement ($p=0.029$), with the other statistically relevant parameters being COPD, presence of

Table 2 Laboratory results, intensive care scoring systems, and outcome comparison of patients

Parameters (mean, ±SD)		Below 65 Years (*n = 353*) *(n,%)*	Above 65 Years (*n = 756*) *(n,%)*	Total (*n =* 1109) *(n,%)*	*p*-value
Uric Acid*(mg/dl)*		5.25 (2.18)	5.95 (2.79)	5.73 (2.41)	**0.001**
Creatinine*(mg/dl)*		0.83 (0.26)	1.00 (0.35)	0.95 (0.33)	**0.001**
Blood Urea Nitrogen*(mg/dl)*		19.79 (9.23)	25.50 (11.48)	23.65 (11.12)	**0.001**
Glomerular Filtration Rate*(ml/min/1.73 m^2)*		91.79 (23.27)	68.52 (23.50)	75.88 (25.8)	**0.001**
Sodium*(mmol/L)*		138.79 (3.64)	139.41 (4.07)	139.21 (3.95)	**0.001**
Potassium*(mmol/L)*		4.42 (0.59)	4.36 (0.69)	4.38 (0.66)	0.146
Calcium*(mg/dl)*		8.79 (0.60)	8.59 (0.64)	8.66 (0.64)	**0.001**
Chloride*(mmol/L)*		96.56 (5.33)	98.17 (5.55)	97.66 (5.55)	**0.001**
Magnesium*(mg/dl)*		1.99 (0.36)	1.97 (0.34)	1.98 (0.35)	0.425
Albumin (g/dl)		33.5 (5.4)	31.0 (5.6)	31.8 (5.6)	**0.001**
Arterial Blood Gas Results					
pH		7.4 (0.07)	7.40 (0.08)	7.41 (0.08)	0.989
Partial carbon dioxide*(mmHg)*		60.1 (15.98)	56.97 (15.09)	57.97 (15.44)	**0.02**
Bicarbonate*(mEq/L)*		36.56 (7.80)	34.56 (7.85)	35.2 (7.89)	0.001
Intensive Care Scoring Systems					
Glasgow Coma		14.97 (0.19)	14.94 (0.30)	14.95 (0.27)	0.036
APACHE II		13.08 (3.70)	15.92 (3.7)	15.02 (3.93)	**0.001**
SOFA Score		1.61 (0.95)	1.90 (1.09)	1.81 (1.06)	**0.001**
Non-Invasive Mechanical Ventilation *(n,%)*	*Not Required*	110 (31.2)	257 (34.1)	367 (33.2)	0.336
	Required	243 (68.8)	497 (65.9)	740 (66.8)	
Outcome*(n,%)*	*Exitus*	23 (6.5)	62 (8.2)	85 (7.7)	0.004
	Discharge	262 (74.2)	483 (63.9)	745 (67.2)	
	Admission to Ward	41 (11.6)	109 (14.4)	150 (13.5)	
	Admission to another ICU	27 (7.6)	102 (13.5)	129 (11.6)	

SD: Standard Deviation; **SOFA**: Sequential Organ Failure Assessment; **ICU**: Intensive Care Unit. The exitus definition included the patients who were accepted as exitus within the ICU setting. For outcome association, the Cramer V value was 0.109, and thus the magnitude of association was accepted as small

Table 3 Correlation analysis of parameters for intensive care unit scores, NIMV requirement, and outcome for patients below 65 years old

Parameters		Geriatric Patients (> 65 years)					
		Glasgow Coma	APACHE II	SOFA	NIMV Requirement	Outcome	Mortality
Uric Acid	*CC*	-0.057	0.081	**0.149****	0.054	-0.069	0.051
	P value	0.295	0.134	**0.006**	0.316	0.104	0.345
Hospitalization Duration	*CC*	0.003	0.005	-0.001	0.052	-0.051	-0.089
	P value	0.955	0.932	0.993	0.337	0.247	0.098
COPD	*CC*	0.063	**-0.146****	**-0.185****	**0.387****	**-0.409****	**-0.273****
	P value	0.236	**0.006**	**0.001**	**0.001**	**0.001**	**0.000**
Pneumonia	*CC*	0.049	0.046	0.029	**-0.273****	**0.178****	0.007
	P value	0.361	0.393	0.592	**0.001**	**0.002**	0.896
Diabetes Mellitus	*CC*	-0.042	0.051	-0.041	-0.001	0.002	-0.002
	P value	0.430	0.345	0.442	0.994	0.987	0.965
Interstitial Lung Disease	*CC*	0.027	0.039	0.098	**-0.177****	**0.278****	**0.123***
	P value	0.609	0.469	0.068	**0.002**	**0.001**	**0.021**
Lung Malignancy	*CC*	-0.023	**0.186****	0.086	**-0.110***	**0.439****	**0.430****
	P value	0.671	**0.001**	0.109	**0.039**	**0.001**	**0.000**
PE	*CC*	**-0.125***	-0.008	**0.189****	**-0.239****	**0.103***	0.064
	P value	**0.019**	0.874	**0.001**	**0.001**	**0.045**	0.231
Congestive Heart Failure	*CC*	0.018	0.027	**0.123***	-0.053	-0.073	-0.035
	P value	0.741	0.617	**0.021**	0.316	0.151	0.516
Atrial Fibrillation	*CC*	0.023	0.056	-0.039	**-0.106***	-0.012	0.024
	P value	0.667	0.292	0.466	**0.046**	0.809	0.652
Bronchiectasis	*CC*	0.023	-0.018	-0.075	-0.033	-0.001	-0.045
	P value	0.667	0.741	0.160	0.542	0.998	0.398
Creatinine	*CC*	-0.093	**0.108***	**0.172****	-0.031	-0.049	-0.059
	P value	0.086	**0.048**	**0.001**	0.566	0.251	0.280
Blood Urea Nitrogen	*CC*	-0.024	**0.204****	**0.230****	0.078	**0.104***	**0.171****
	P value	0.657	**0.001**	**0.001**	0.149	**0.016**	**0.001**
GFR	*CC*	0.099	**-0.247****	**-0.349****	-0.004	0.075	0.027
	P value	0.065	**0.001**	**0.001**	0.937	0.077	0.612
Sodium	*CC*	-0.077	-0.071	-0.031	0.061	-0.071	-0.086
	P value	0.150	0.187	0.564	0.255	0.103	0.108
Potassium	*CC*	0.040	-0.080	-0.024	**0.182****	**-0.112****	0.026
	P value	0.457	0.133	0.658	**0.002**	**0.008**	0.623
Calcium	*CC*	0.017	**-0.112***	**-0.198****	0.080	**-0.120****	**-0.137***
	P value	0.748	**0.038**	**0.001**	0.135	**0.006**	**0.011**
Chloride	*CC*	-0.048	0.061	0.100	**-0.340****	0.050	0.032
	P value	0.375	0.255	0.061	**0.001**	0.246	0.547
Magnesium	*CC*	-0.072	0.026	0.046	0.019	0.007	0.050
	P value	0.203	0.650	0.413	0.739	0.876	0.373
Albumin	*CC*	0.025	**-0.244****	**-0.179****	0.082	**-0.284****	**-0.274****
	P value	0.637	**0.001**	**0.002**	0.123	**0.001**	**0.000**
pH	*CC*	0.004	**-0.117***	-0.065	**-0.373****	0.079	0.027
	P value	0.934	**0.028**	0.226	**0.001**	0.063	0.608
Partial carbon dioxide	*CC*	0.010	-0.034	-0.089	**0.625****	**-0.191****	-0.091
	P value	0.856	0.531	0.096	**0.001**	**0.001**	0.087
Bicarbonate	*CC*	0.002	**-0.132***	**-0.152****	**0.502****	**-0.172****	-0.093
	P value	0.968	**0.013**	**0.004**	**0.001**	**0.001**	0.082

CC: Correlation Coefficient; SD: Standard Deviation; COPD: Chronic Obstructive Pulmonary Disease; GFR: Glomerular Filtration Rate; SOFA: Sequential Organ Failure Assessment; NIMV: Non-Invasive Mechanical Ventilation; PE: Pulmonary Thromboembolism. For outcome comparison, Kendall's Tau B association was utilized, while Spearman's correlation made the remaining comparison

Table 4 Correlation analysis of parameters for intensive care unit scores, NIMV requirement and outcome for patients above 65 years old

Parameters		Geriatric Patients (> 65 years)					
		Glasgow Coma	APACHE II	SOFA Score	NIMV Requirement	Outcome	Mortality
Uric Acid	*CC*	-0.050	**0.164****	**0.266****	**0.125****	-0.049	-0.003
	P value	0.183	**0.001**	**0.001**	**0.002**	0.090	0.929
Hospitalization Duration	*CC*	0.029	-0.019	-0.023	0.028	**-0.159****	0.009
	P value	0.430	0.600	0.534	0.456	**0.001**	0.814
Chronic Obstructive Pulmonary Disease	*CC*	0.045	**-0.098****	**-0.114****	**0.353****	**-0.259****	**-0.167****
	P value	0.217	**0.007**	**0.002**	**0.001**	**0.001**	**0.000**
Pneumonia	*CC*	**-0.100****	0.070	0.020	**-0.282****	**0.203****	**0.097****
	P value	**0.006**	0.054	0.590	**0.001**	**0.001**	**0.008**
Diabetes Mellitus	*CC*	-0.005	-0.016	-0.024	0.001	-0.011	0.023
	P value	0.882	0.664	0.512	0.995	0.744	0.530
Interstitial Lung Disease	*CC*	0.044	-0.018	0.003	**-0.148****	**0.138****	**0.105****
	P value	0.231	0.621	0.925	**0.001**	**0.001**	**0.004**
Lung Malignancy	*CC*	**-0.083***	**0.078***	**0.114****	-0.051	**0.123****	0.069
	P value	**0.023**	**0.034**	**0.002**	0.161	**0.001**	0.058
Pulmonary Thromboembolism	*CC*	0.039	-0.025	-0.031	**-0.175****	-0.060	-0.013
	P value	0.288	0.502	0.392	**0.001**	0.080	0.717
Congestive Heart Failure	*CC*	-0.043	-0.020	0.071	-0.024	-0.025	-0.042
	P value	0.242	0.592	0.051	0.511	0.467	0.253
Atrial Fibrillation	*CC*	0.032	-0.055	-0.022	0.020	**-0.073***	-0.021
	P value	0.385	0.130	0.539	0.589	**0.034**	0.561
Bronchiectasis	*CC*	-0.019	-0.047	-0.069	0.002	0.010	-0.033
	P value	0.598	0.196	0.059	0.962	0.765	0.368
Creatinine	*CC*	-0.015	**0.276****	**0.365****	-0.006	-0.041	0.011
	P value	0.688	**0.001**	**0.001**	0.871	0.154	0.768
Blood Urea Nitrogen	*CC*	-0.032	**0.217****	**0.335****	-0.012	0.016	0.062
	P value	0.391	**0.001**	**0.001**	0.754	0.590	0.099
Glomerular Filtration Rate	*CC*	**0.086***	**-0.278****	**-0.402****	0.010	0.006	-0.008
	P value	**0.019**	**0.001**	**0.001**	0.789	0.831	0.816
Sodium	*CC*	**-0.099****	-0.056	0.064	**0.138****	-0.014	-0.006
	P value	**0.007**	0.128	0.082	**0.001**	0.623	0.862
Potassium	*CC*	**0.133****	-0.029	-0.025	**0.133****	**-0.140****	**-0.125****
	P value	**0.001**	0.429	0.486	**0.001**	**0.001**	**0.001**
Calcium	*CC*	**0.083***	-0.072	**-0.151****	**0.108****	**-0.128****	**-0.099****
	P value	**0.025**	0.052	**0.001**	**0.003**	**0.001**	**0.007**
Chloride	*CC*	-0.035	**0.119****	**0.153****	**-0.243****	**0.082****	0.008
	P value	0.339	**0.001**	**0.001**	**0.001**	**0.005**	0.829
Magnesium	*CC*	0.045	0.050	0.041	-0.009	-0.039	-0.027
	P value	0.244	0.192	0.293	0.805	0.208	0.484
Albumin	*CC*	**0.123****	**-0.077***	**-0.158****	**0.215****	**-0.274****	**-0.230****
	P value	**0.002**	**0.035**	**0.001**	**0.001**	**0.001**	**0.000**
pH	*CC*	-0.038	**-0.090***	-0.050	**-0.438****	**0.095****	**0.090***
	P value	0.303	**0.015**	0.170	**0.001**	**0.002**	**0.013**
Partial carbon dioxide	*CC*	0.057	**-0.087***	-0.072	**0.629****	**-0.163****	**-0.084***
	P value	0.119	**0.017**	0.051	**0.001**	**0.001**	**0.022**
Bicarbonate	*CC*	0.047	**-0.167****	**-0.175****	**0.409****	**-0.108****	-0.013
	P value	0.197	**0.001**	**0.001**	**0.001**	**0.001**	0.725

CC: Correlation coefficient; SD: Standard Deviation; SOFA: Sequential Organ Failure Assessment; NIMV: Non-Invasive Mechanical Ventilation. For outcome comparison, Kendall's Tau B association was utilized, while the remaining comparison was made by Spearman's correlation

Table 5 Regression analysis of parameters correlated with Non-invasive mechanical ventilation requirement

Parameters	Estimated Coefficient	Standard Error	Wald	*p*-value	Odds Ratio	95% C.I. for Odds Ratio	
						Lower	Upper
Uric Acid	0.120	0.055	4.761	**0.029**	1.127	1.012	1.255
COPD	0.720	0.264	7.457	**0.006**	2.055	1.225	3.447
Pneumonia	-1.013	0.308	10.850	**0.001**	0.363	0.199	0.663
ILD	-0.313	0.524	0.357	0.550	0.731	0.262	2.042
PE	-1.249	0.627	3.972	**0.046**	0.287	0.084	0.980
Sodium	0.013	0.041	0.092	0.762	1.013	0.934	1.098
Potassium	0.000	0.211	0.000	0.999	1.000	0.661	1.513
Calcium	-0.018	0.240	0.006	0.939	0.982	0.614	1.571
Chloride	-0.051	0.034	2.295	0.130	0.950	0.889	1.015
Albumin	-0.022	0.030	0.554	0.457	0.978	0.922	1.037
pH	-7.242	4.107	3.109	0.078	0.001	0.000	2.244
PCO_2	0.113	0.034	11.360	**0.001**	1.120	1.049	1.196
HCO_3	0.036	0.052	0.485	0.486	1.037	0.936	1.149

C.I.: Confidence Interval; **COPD**: Chronic Obstructive Pulmonary Disease; **ILD**: Interstitial Lung Disease; **PE**: Pulmonary Thromboembolism; **PCO_2**: Partial carbon dioxide; **HCO_3**: Bicarbonate

pneumonia, PE, and PCO_2 levels (p equal to 0.006, 0.001, 0.046, and 0.01 respectively) (Table 5).

Discussion

The impact of serum uric acid (SUA) levels on respiratory function becomes more evident in the geriatric population. An observation that supported the fact that uric acid had a different role in the elderly compared to the other group was that, in correlation analysis, there was not any significant correlation between uric acid levels and NIV requirement among the non-elderly population. The elderly group, on the other hand, showed a positive correlation. Additionally, despite the distribution of respiratory failure types being the same between the two groups and the elderly group having lower CO_2 levels, the correlation between uric acid and NIV requirement was only present in the elderly group. This observation was strengthened by the regression analysis, in which COPD, as expected, had a significant role in NIV requirement; however, even in this model, uric acid levels were still significant in their role of NIV requirement prediction. Overall these observations support the role of uric acid in respiratory failure of elderly population.

When evaluated as two groups, below 65 years old and above, some parameters had significant differences between them, such as hospitalization duration, lung malignancy, and bronchiectasis. However, regarding respiratory failure type and possible factors affecting it, mainly COPD and ILD, the two groups did not have a significant difference. These observations support that both groups' respiratory support requirements were similar. Another important observation was that the elderly population varied regarding electrolyte evaluation, in which a higher creatinine, uric acid, blood urea nitrogen, and a lower albumin level were noted. As an expected finding, the elderly population had a worse outcome than those younger than 65, with worse APACHE II and SOFA scores.

Respiratory failure remains a major cause of mortality, with further care required in advanced age due to possible serious outcomes that could be remedied with close attention. Therefore, in addition to scoring systems that predict mortality, identifying clinical characteristics and easily accessible biomarkers are also required for patients' treatment modalities. A study investigating the prognostic role of hyperuricemia in patients with COPD demonstrated that COPD patients with hyperuricemia had a higher risk of mortality compared to normouricemic patients [7]. Previous research has shown that UA holds particular importance in the human body due to its antioxidant properties [8, 9]. However, some studies have also stated the opposite effect of UA also has the opposite effect, acting as a pro-inflammatory factor, particularly in individuals with high serum UA levels [10, 11].

Bartziokas and colleagues conducted a study on the clinical significance of serum uric acid levels at the time of patient admission. They found that serum uric acid levels at the time of presentation due to acute exacerbations of COPD (AECOPD) were an independent predictor of 30-day mortality and were associated with a higher risk of AECOPD and hospitalization due to AECOPD during one-year follow-up. Additionally, this study demonstrated that patients with elevated uric acid levels required extended hospital stays, were more frequently admitted to the ICU, and required non-invasive mechanical ventilation (NIV) during their hospital course [12].

Recent studies continue to support the role of serum uric acid (SUA) as a prognostic biomarker in respiratory failure, particularly among patients with COPD. A recent prospective cohort study highlighted that elevated

SUA levels were significantly associated with advanced-stage COPD and severe airflow obstruction. This suggests that SUA is a cost-effective biomarker for assessing disease severity and prognosis in acute exacerbations of COPD [13]. A meta-analysis also confirmed that SUA levels increase with the severity of COPD, particularly in patients categorized under GOLD stages 3 and 4, emphasizing SUA's potential in disease stratification [14]. Furthermore, elevated SUA levels have been linked to worse clinical outcomes during acute exacerbations, including longer hospital stays, increased ICU admissions, and higher mortality rates [15]. These findings reinforce the importance of monitoring SUA in respiratory failure patients, particularly in older populations where hyperuricemia is more prevalent and may exacerbate disease progression.

Various mechanisms may play a role in the presence of elevated uric acid levels in respiratory failure. First, prolonged hypoxemia, which worsens during acute respiratory failure, may lead to increased pulmonary artery pressures, resulting in increased right ventricular afterload, promoting purine degradation through increased xanthine oxidase activity [16]. Second, a significant portion of respiratory failure patients have concomitant cardiovascular disease, which may be associated with elevated uric acid levels [17]. Third, impaired lung function reduces oxygen intake, causing tissue hypoxia, which is more pronounced during respiratory failure, leading to elevated circulating uric acid levels due to both lung and peripheral tissue damage [18]. Overall, these processes eventually increase uric acid levels, which is more evident in the elderly population.

The correlation between uric acid and NIV support requirement is another topic of interest, due to the higher respiratory dysfunction present in patients requiring NIV support. A study by Zhang and colleagues demonstrated that hyperuricemia in COPD patients is associated with early mortality. This study reported that hyperuricemic patients have a higher risk of mortality compared to normouricemic patients, which was a similar finding to other studies; however, this study additionally reported that a higher mortality was particularly evident among patients requiring NIV [7]. Our findings remain similar to the mentioned study, as it was stated that unlike the general population, uric acid had a correlation with NIV requirements among the elderly. It was also shown that hyperuricemia is associated with mortality in the geriatric patient group, highlighting that these patients are more likely to require NIV. Similar to Zhang's study, our study supports the prognostic importance of uric acid.

NIV remains the preferred approach in treating respiratory failure in the geriatric population, aiming to avoid the complications associated with invasive ventilation. However, our study shows that, despite the use of NIV, serum uric acid levels did not decrease in this patient group; in fact, they increased further as the need for NIV intensified. This finding is consistent with the study by Patanwar and colleagues, which demonstrated that elevated serum uric acid levels were associated with longer hospital stays, increased ICU requirements, and higher mortality rates [19]. Patanwar's study reported that hyperuricemic patients had worse clinical outcomes, including increased needs for NIV and intensive care. These similarities suggest that metabolic stress persists in geriatric patients despite the use of NIV.

Previous studies have demonstrated that uric acid levels are associated with lower FVC and FEV_1 values. Garcia-Pachon and colleagues reported that a high uric acid/creatinine ratio was linked to reduced respiratory function [20]. Similarly, in our study, we observed that geriatric patients with elevated serum uric acid levels required more NIV, likely due to age-related respiratory muscle strength loss, although we did not assess their respiratory function. These findings suggest that elevated serum uric acid levels could indicate respiratory dysfunction in geriatric patients and may hold a significant place in clinical management. While NIV has the ability to improve oxygenation by providing respiratory support, our study indicates that oxidative stress cannot be fully controlled in geriatric patients despite this therapy. The study by Embarak and colleagues revealed that elevated serum uric acid levels in patients experiencing COPD exacerbations were associated with increased ICU admissions, the need for mechanical ventilation, and higher mortality rates [21].

Recent studies have helped us better understand the relationship between serum uric acid (SUA) levels, the need for non-invasive ventilation (NIV), and mortality in patients with COPD. In a study by Patanwar et al. [15], it was shown that COPD patients with high serum uric acid levels had longer hospital stays, increased intensive care unit (ICU) admissions, higher requirements for NIV/invasive mechanical ventilation (IMV), and higher mortality rates. Similarly, in a prospective study conducted by Muhammad et al. [22], it was reported that patients experiencing acute COPD exacerbations with elevated serum uric acid levels had a higher risk of mortality and required more NIV support compared to those with normal levels. Our study confirms these findings, showing that oxidative stress and inflammatory processes may persist despite NIV alleviating hypoxemia symptoms through oxygenation in the geriatric population. This could result in a limited response to respiratory therapy in geriatric patients, leading to poorer prognoses. These findings suggest that hyperuricemia is not only associated with increased inflammatory processes but also serves as a crucial biomarker that impacts NIV requirements and clinical outcomes in COPD patients.

Conclusion

In conclusion, high serum uric acid levels in the geriatric patients emerge as a strong prognostic marker associated with increased NIV needs and worse clinical outcomes. Consistent with other studies in the literature, our study found that high serum uric acid levels in the geriatric population become a marker of oxidative stress, and despite NIV, clinical outcomes tend to worsen in this group. Monitoring serum uric acid levels could play a critical role in optimizing respiratory support and managing geriatric patients.

Acknowledgements
We would like to thank Dr Yusuf Tuğrul Şipit for his helpful comments and support.

Author contributions
M.Y., D.Ç., T.Ö., G.E.D., M.D., M.O.C., M.A., K.E., A.C., D.K. have made substantial contributions to the conception. M.Y., D.Ç., T.Ö., G.E.D., M.D., M.O.C., M.A., K.E., A.C., D.K. have made substantial contributions to the design of the work. M.Y., D.Ç., T.Ö., G.E.D., M.D., M.O.C., M.A., K.E., A.C., D.K. have made substantial contributions to the acquisition, analysis, interpretation of data. M.Y., D.Ç., T.Ö., G.E.D., M.D., M.O.C., M.A., K.E., A.C., D.K. have substantively revised it and to have approved the submitted version (and any substantially modified version that involves the author's contribution to the study). M.Y., D.Ç., T.Ö., G.E.D., M.D., M.O.C., M.A., K.E., A.C., D.K. have made substantial contributions to the have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

Funding
No funding. This study received no grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability
The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The Ankara Ataturk Sanatorium Training and Research Hospital's Clinical Research Ethics Committee approved this study with the Ethical Decision Number: 2012-KAEK-15/2790, dated 27.09.2023. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication
This study is a retrospective study based on patients data on files and computer systems. As our hospital is a training and research hospital, at admission, all patients or first-degree relatives were asked to give both written and verbal permission about their anonymous data used for the scientific studies. We excluded any patients or first-degree relatives who did not give consent from this retrospective analysis.

Competing interests
The authors declare no competing interests.

Compliance with ethical standards
All the authors mentioned in the manuscript have agreed to authorship, read and approved the manuscript, and given consent for submission and subsequent publication of the manuscript. The manuscript, in part or in full, has not been submitted or published anywhere.

Clinical trial number
Not applicable.

Author details
[1]Department of Pulmonology, University of Health Sciences, Ankara Ataturk Sanatorium Training and Research Hospital, Sanatoryum St, Kecioren, Ankara 06290, Turkey
[2]Faculty of Medicine, Department of Pulmonology, Alanya Alaaddin Keykubat University, Antalya, Turkey
[3]Department of Anesthesiology and Reanimation, University of Health Sciences, Ankara Ataturk Sanatorium Training and Research Hospital, Ankara, Turkey
[4]Kırıkkale Yuksek Ihtisas Hospital, Kırıkkale, Turkey

Received: 1 January 2025 / Accepted: 17 March 2025
Published online: 29 March 2025

References

1. Moubarez DA. The predictive value of serum uric acid in the development of acute kidney injury and mortality in patients with sepsis. J Nephropathology. 2022. https://doi.org/10.34172/jnp.2022.17307.
2. El-Shebiny EM, Daif S, Shoeib S, Fathi Y, Zahran E. Serum uric acid level as a prognostic factor in sepsis outcome. Egypt J Chest Dis Tuberculosis. 2022;71:20–5. https://doi.org/10.4103/ejcdt.ejcdt_3_20.
3. Watanabe T, Ishikawa M, Abe K, Ishikawa T, Imakiire S, Masaki K, Hosokawa K, Fukuuchi T, Kaneko K, Ohtsubo T, Hirano M, Hirano K, Tsutsui H. Increased lung uric acid deteriorates pulmonary arterial hypertension. J Am Heart Assoc. 2021;10(23):e022712. Epub 2021 Nov 30. PMID: 34845934; PMCID: PMC9075373.
4. Yin Y, Chou C-A. (2022). Early ICU mortality prediction for respiratory failure by a regression-based hazard Markov model. *44th Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), 2651–2654.*https://doi.org/10.1109/EMBC48229.2022.9871309
5. Seğmen F, Uysal E, Erdem D. (2022). The role of hyperuricemia in acute renal failure. *Intensive Care Journal.*https://consensus.app/papers/the-role-of-hyperuricemia-in-acute-renal-failure-seğmen-uysal/e2b37ed00eb1592a81b37f33fe3ab346/?utm_source=chatgpt
6. Xiao Q, Zhou Q, Shen W, Dong S, Tan Y, Zhang X, Yao L, Li Q, Qin Z, Wang T. Blood Urea nitrogen-to-albumin ratio independently predicts 30-day mortality in acute respiratory failure patients: A retrospective cohort study. J Thorac Disease. 2024;16:4892–903. https://doi.org/10.21037/jtd-24-298.
7. Zhang X, Liu L, Liang R, Jin S. Hyperuricemia is a biomarker of early mortality in patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2015;10:2519–23. https://doi.org/10.2147/COPD.S87202. PMID: 26648710; PMCID: PMC4664430.
8. Rock KL, Kataoka H, Lai JJ. Uric acid as a danger signal in gout and its comorbidities. Nat Rev Rheumatol. 2013;9(1):13–23.
9. Alvarez-Lario B, Macarron-Vicente J. Is there anything good in uric acid? QJM. 2011;104(12):1015–24.
10. Bardin T, Richette P. Definition of hyperuricemia and gouty conditions. CurrOpinRheumatol. 2014;26(2):186–91.
11. Ghaemi-Oskouie F, Shi Y. The role of uric acid as an endogenous danger signal in immunity and inflammation. CurrRheumatol Rep. 2011;13(2):160–6.
12. Bartziokas K, Papaioannou AI, Loukides S, Papadopoulos A, Haniotou A, Papiris S, Kostikas K. Serum uric acid as a predictor of mortality and future exacerbations of COPD. EurRespir J. 2014;43(1):43–53. doi: 10.1183/09031936.00209212. Epub 2013 May 3. PMID: 23645404.
13. Soman M, Chakkamadathil J, Noorayingarath H, Lal A. Serum uric acid as a biomarker in patients admitted with acute exacerbation of chronic obstructive pulmonary disease to a tertiary hospital, Kerala. J Adv Lung Health. 2024. https://doi.org/10.4103/jalh.jalh_25_24.).
14. Li H, Chen Y. Serum uric acid level as a biomarker for chronic obstructive pulmonary disease: a meta-analysis. J Int Med Res. 2021;49. https://doi.org/10.1177/0300060520983705.
15. Patanwar S, Chakraborti A, Kumar L, Vohra V, Tayal D. Serum uric acid and clinical outcome of patients with acute exacerbation of chronic obstructive pulmonary disease. Med J Dr D Y Patil Vidyapeeth. 2020;13:658–64. https://doi.org/10.4103/mjdrdypu.mjdrdypu_261_19.

16. Pascual-Figal DA, Hurtado-Martinez JA, Redondo B, et al. Hyperuricaemia and long-term outcome after hospital discharge in acute heart failure patients. Eur J Heart Fail. 2007;9:518–24.
17. Hunninghake DB. Cardiovascular disease in chronic obstructive pulmonary disease. Proc Am ThoracSoc. 2005;2:44–9.
18. Fabbri LM, Rabe KF. From COPD to chronic systemic inflammatory syndrome? Lancet. 2007;370:797–9.
19. Patanwar S, Chakraborti A, Kumar L, Vohra V, Tayal D. Serum uric acid and clinical outcome of patients with acute exacerbation of chronic obstructive pulmonary disease. Med J DY PatilVidyapeeth. 2020;13(6):658–64. https://doi.org/10.4103/mjdrdypu.mjdrdypu_261_19.
20. Garcia-Pachon E, Padilla-Navas I, Shum C. Serum uric acid to creatinine ratio in patients with chronic obstructive pulmonary disease. Lung. 2007;185(1):21–4. https://doi.org/10.1007/s00408-007-9032-6.
21. Embarak S, Sileem AE, Abdrabboh M, Mokhtar A. Serum uric acid as a biomarker for prediction of outcomes of patients hospitalized for acute exacerbation of chronic obstructive pulmonary disease. Egypt J Bronchol. 2014;8(2):115–20. https://doi.org/10.4103/1687-8426.139580.
22. Muhammad J, Coll M, Sajjad I, Mehr A, Imran. Elevated levels of serum uric acid and its correlation with unfavorable out-comes in individuals who experience acute exacerbation of chronic obstructive airway disease. JMMC. 2023;3https://doi.org/10.62118/jmmc.v14i1.276.

Publisher's note