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IS INCREASED URIC ACID LEVEL A RISK FACTOR FOR MORTALITY?

Pediatrics

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ABSTRACT

Objective: To determine the relationship between serum uric acid level and prognosis of patients admitted to pediatric intensive care unit (PICU).

Methods: Patients admitted to pediatric intensive care unit between January 2017 and January 2018 were enrolled. Sex, age, body weight, diagnosis, Pediatric Risk of Mortality (PRISM) score, mechanical ventilator (MV) need, number of days of mechanical ventilator, prognosis, presence of sepsis, admission serum uric acid and creatinine levels were recorded.

Results: This study included a total of 116 patients. Of the patients, 53.4% were provided respiratory support with mechanical ventilator. 15.5% of them died. There was a significant correlation between serum uric acid level and PRISM score (p:0.000; p<0.05). There was no significant correlation between mean serum uric acid level and the duration of intensive care unit stay, prognosis, and the number of days on MV (p>0.05). The mortality rate was 11.4% among patients who had a uric acid level between 2.6 and 7 mg/dL, while the mortality reached 50% among those with a uric acid level above 7 mg/dL (p:0.016; p<0.05). Patients with sepsis had a serum uric acid level that was significantly higher than those without sepsis (4.6±2.8 vs 3.51±1.7; p:0.014).

Conclusion: serum uric acid level at PICU admission is not a suitable marker for mortality. However, it may play a role as an additional risk factor among patients with sepsis and a uric acid level ≥7 mg/dL.

KEYWORDS

INTRODUCTION

Uric acid is a product of the purine metabolism in humans, and a major water-soluble endogenous antioxidant. Serum uric acid level is affected by many factors such as excessive production, reduced glomerular filtration rate, renal hypoperfusion, increased tubular reabsorption, and reduced elimination. Recently, increased uric acid levels are considered to play a role as a prooxidant and a potential risk factor for mortality in renal disease, hypertension, cardiovascular disorders, diabetes mellitus, stroke, cancer, and obesity (1,2). There are also studies indicating that increased serum uric acid levels are a predictor of mortality among pediatric patients (3,4).

The aim of the present study was to assess the relationship between serum uric acid level and the prognosis of patients admitted to pediatric intensive care unit.

METHODS

This study was approved by Ümraniye TRH. It enrolled patients admitted to a 10-bed tertiary pediatric intensive care unit between January 2017 and January 2018. It excluded patients who had renal failure and those admitted for less than 24 hours. Sex, age, body weight, diagnosis, Pediatric Risk of Mortality (PRISM) score, mechanical ventilator need, number of days of mechanical ventilator, prognosis, presence of sepsis, admission serum uric acid and creatinine levels were recorded.

RESULTS

The study enrolled a total of 116 patients, 53 of whom (45.7%) were female and 63 (54.3%) were male. The mean age of the study population was 71.5±76.3 months; the mean body weight was 21.0±19.5 kg; the mean PRISM score was 11.6±8.5; the mean duration of intensive care stay was 17.5±21.9 days; the mean number of days on MV was 18.6±24.0. Of the patients, 53.4% were provided respiratory support with mechanical ventilator. 15.5% of them died. Sepsis was present in 49.1% of the patients; 58.1% of the patients had a serum uric acid level range of 2.6 to 7 mg/dL, and 25% had a level below 2.5 mg/d L, and 6.9% had levels above 7 mg/dL (Table 1).

In terms of diagnosis on admission to intensive care, the largest group consisted of respiratory diseases (27 cases), followed by neurological diseases (25 cases) and cardiac diseases (18 cases) (Table 2). There was a significant positive correlation at a level of 38.5% between serum uric acid level and PRISM score (p:0.000; p<0.05) (Figure 1).

There was no significant correlation between mean serum uric acid levels and the duration of intensive care unit stays, prognosis, and the number of days on MV (p>0.05) (Table 3). The mortality rate was 11.4% among patients who had a uric acid level between 2.6 and 7 mg/dL, while it was 50% among those with a uric acid level above 7 mg/dL (p:0.016; p<0.05) (Table 3). Patients with sepsis had a serum uric acid level that was significantly higher than those without sepsis (4.6±2.8 vs 3.51±1.7; p:0.014).

DISCUSSION

This study did not reveal any significant relationship between serum uric acid level and duration of intensive care unit stay, prognosis, and duration of MV. However, it was shown that patients with sepsis had a higher serum uric acid level than those without, and that patients with a serum uric acid level of ≥7 mg/dL had a mortality rate reaching 50%. There was a significant correlation between serum uric acid and PRISM score. Similarly, in a pediatric population, Hooman et al. (3) reported that serum uric acid level measured at PICU admission was not an independent risk factor for mortality. In that study a PRISM score of >38 increased mortality by 1.4 times and the sepsis by 4 times.

Molinos et al. (5) reported that serum uric acid level was an indicator of disease severity particularly among pediatric patients with meningococcal infection. They found out that deceased patients had a mean admission serum uric acid level of 8.2 mg/dl, and those who improved without sequela had a mean serum uric acid level of 1.84 mg/dL (P<0.003). we also found that the patients with sepsis had significantly greater serum uric acid level (4.6±2.82 mg/dL) than those without (3.51±1.7 mg/dL).

Serum uric acid level may cause renal vasoconstriction, impaired autoregulation, proinflammatory and anti-angiogenic properties, and acute kidney injury (AKI), and may play a role in immune response (6,7). In a study comprising 190 adult patients a serum uric acid level of ≥7 was associated with a 35-fold increase in AKI risk, and increased the duration of hospital stay and mechanical ventilation (8). Ejazz et al. (9), in a similar study, a serum uric acid level of ≥6 increased AKI risk by 6 folds, and increased duration of hospital stay. Another study on adult patients with chronic renal disease undergoing cardiac surgery showed that prophylactically administered vitamin E and allopurinol shortened stay at intensive care unit (10). It was shown that reduced serum uric acid level reduced the levels of systemic inflammatory markers such as high-sensitive C-reactive protein and tumor necrosis factor-α (11).

Previous studies have indicated an association between uric acid levels and coronary and cerebrovascular ischemic events. It has been demonstrated that hyperuricemia was associated with multiple risk factors such as obesity, hypertension, reduced HDL cholesterol, hypertriglyceridemia, hyperinsulinemia, and increased insulin resistance, and thus caused an increase in the risk of stroke (12-14). Possible mechanisms include renin increase, reduced nitric oxide, interstitial inflammation and fibrosis, afferent arteriolopathy, increased reactive oxygen species, vascular inflammation, and

vascular smooth muscle proliferation associated with suppressed endothelial cell growth. Furthermore, it was reported that clinically high uric acid levels are an indicator of developing hypertension; that hyperuricemia is present in about 25-60% of untreated cases of hypertension and approximately 90% of hypertensive adolescents; and that reducing uric acid level with treatment exerts antihypertensive effect among patients recently diagnosed with hypertension (15).

The limitations of our study included its single-center and retrospective design, and the lack of an assessment of the relationship between hypertension and AKI.

In conclusion, serum uric acid level at PICU admission is not a suitable marker for mortality. However, it may play a role as an additional marker among patients with sepsis and a uric acid level of ≥7 mg/dL.

TABLE 1: Admission clinical and laboratory parameters

		Min-Max	Mean±SD
Sex $_{n,\%}$	**Female**	53	45.7
	Male	63	54.3
Age (months)		2-253	71.56±76.33
Body weight (kg)		3-83	21.03±19.59
PRISM score		1-40	11.68±8.57
Serum BUN (mg/dL)		5-44.6	19.78±9.36
Serum uric acid (mg/dL)		1-14.4	4.04±2.37
Serum creatinine (mg/dL)		0.28-0.81	0.47±0.11
Duration of intensive care stay (days)		2-135	17.59±21.91
Duration of mechanical ventilation (days)		1-120	18.67±24.03
Need for MV $_{n,\%}$	**Yes**	62	53.4
	No	54	46.6
Sepsis $_{n,\%}$	**Yes**	57	49.1
	No	59	50.9
Serum uric acid (mg/dL) $_{n,\%}$	**≤2.5**	29	25
	2.6-7	79	68.1
	≥7	8	6.9
Prognosis $_{n,\%}$	**Survived**	98	84.5
	Died	18	15.5

PRISM: Pediatric Risk of Mortality, MV: Mechanical ventilation

TABLE 2. Admission diagnosis

Pulmonary disease	27	23.2
Neurologic disease **Cardiac disease** **Oncologic disease**	25 18 14	21.6 15.6 12.0
Trauma **Gastroenterological disease**	10 7	8.7 6.0
Others	15	12.9

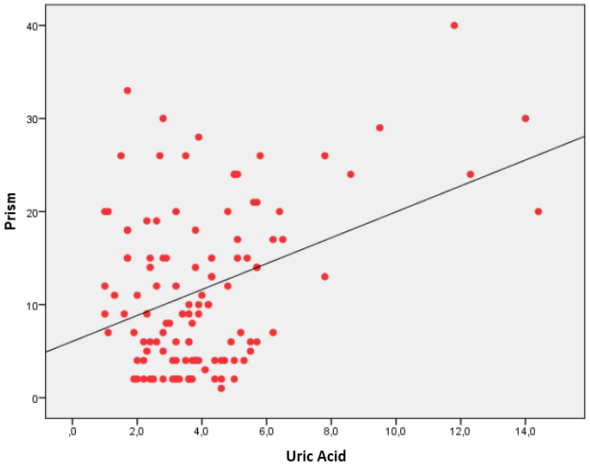

FIGURE 1. Serum uric acid and PRISM score

TABLE 3. The relationship between serum uric acid level and need for mechanical ventilation, the presence of sepsis, and prognosis

		Uric acid level
		Mean±SD
Need for MV	**Yes**	4.1±2.72 mg/dL
	No	3.97±1.92 mg/dl
	p	**0.769**
Prognosis	**Survived**	3.88±1.99
	Died	4.95±3.8
	p	**0.256**
Sepsis	**Yes**	4.6±2.82
	No	3.51±1.7
	p	**0.014***

Student t Test *$p<0.05$

TABLE 4. The relationship between uric acid level and prognosis

Prognosis	**Uric acid level**			**p**
	≤2.5mg/dL	**2.6-7mg/dL**	**≥7mg/dL**	
Survived	24 (82.8%)	70 (88.6%)	4 (50%)	**0.020**
Died	5 (17.2%)	9 (11.4%)	4 (50%)	

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