ORIGINAL RESEARCH PAPER

Medical Biochemistry

A STUDY OF URIC ACID AS AN EARLY PREDICTOR FOR SEVERITY OF SEPSIS IN ICU.

KEY WORDS: Uric acid, AKI, Sepsis.

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ABSTRACT

Introduction: Sepsis is a grave medical illness characterized by a whole-body inflammatory state (systemic inflammatory response syndrome). Third International Consensus Definitions agreeing that sepsis is a deregulated host response to infection that clues to acute organ dysfunction. Septic shock is defined as a problem of sepsis resultant in imbalances in circulatory and metabolic pathways in the body. Increased levels of serum uric acid causes acute beginning of many transcription factors in patients with severe infection and is a poor prognostic sign in case of severe infection. A chronic condition is also related with elevated serum uric acid. **Aim**: To study the correlation between hyperuricemia and mortality and morbidity in patients with clinically diagnosed sepsis. **Material And Methods:** This research is carried out as a prospective cohort study in clinically assumed sepsis patients with age more than 18 years, in medical intensive care unit in Rama Medical College and Research Centre, Hapur from January 2022 till June 2022. Once the patient met the inclusion criteria blood samples were obtained. The primary end point was correlation between hyperuricemia in clinically suspected sepsis patients and morbidity and mortality rate. **Result:** Among the 62 sepsis patients, 35 patients had hyperuricemia. The mortility of sepsis in the hyperuricemia group showed significantly statistical difference. **Conclusion:** This study demonstrates that serum uric acid may be potentially used as a marker of severity of illness as well as predictor of mortality and morbidity in Patients with clinically diagnosed sepsis in the ICU.

INTRODUCTION

Sepsis term is coined from the Greek word sepo meaning decay or putrefaction. Septic shock was derived from the French word choquer meaning 'to collide with'.

Sepsis Definitions Conference was convened in 2001 under the auspices of ACCP, SCCM, the European Society of Intensive Care Medicine, and the Surgical Infection Societies re-visited the definitions of sepsis and related conditions. The key change was regarding the definition of systemic inflammatory response syndrome (SIRS) [manifested by (but not limited to) 2 or more of the following conditions: temperature> 38 °C or, < 36 °C; heart rate > 90 beats/min; respiratory rate >20/min or (PaCO2) < 32 mmHg; white blood cell count >12.0 ×109/L, < 4:0 × 109/L, or > 10% immature (band) forms] which was expanded to include longer list of possible signs of sepsis. As per the new guidelines, sepsis is defined as infection plus systemic manifestations of infection. Severe sepsis is defined as sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion. Septic shock is defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation. Equally community acquired and hospital acquired infections can cause sepsis. Pneumonia is the most common cause of sepsis which is found in about half of all cases followed by intra-abdominal and genitourinary infections as the next common causes. In the United States, current cohort studies using administrative data suggest that upwards of 2 million cases of sepsis occur annually. Shock is present in ~30% of cases. The incidences of sepsis and septic shock also reported to be increasing (according to ICD9-CM diagnosis and procedure codes), with a rise of almost 50% in the past decade. In India, a recent study involving 5 years duration in a hospital, it was found that the mortality among sepsis patients was 63.6% out of which 56% died in the ICU. Since long time, the clinical features of sepsis were considered to be the result of an excessive inflammatory host response (SIRS). Generally, pro inflammatory reactions are responsible for "collateral" tissue damage in sepsis, whereas anti-inflammatory response is instituted in the enhanced susceptibility to secondary infections which occur later in the course. These mechanisms can be characterised by direct damage to organs by the microbes and damage to organs arising from the host's immune response. The ability of the host to resist as well as tolerate direct, pathological and immunologic damage will determine whether uncomplicated infection becomes sepsis. Humans convert adenosine and guanosine to uric acid. Adenosine is first converted to inosine by adenosine deaminase. In mammals, other than higher primates, uric acid is converted to water soluble product allantoin by uricase enzyme. As humans lack uricase, uric acid is the end product of purine catabolism in human beings. The enzyme involved in the formation of uric acid is xanthine oxidase. The daily synthesis rate is estimated to be 1.8 mmol, with a total body pool of approximately 7.2 mmol (1200 mg in adult males and about one half that in females) Approximately 70% of uric acid will be excreted by kidneys. The remaining 30% is excreted by the gastrointestinal tract. Additionally, some uric acid is degraded after reaction with oxidants or peroxynitrite. Uric acid is predominantly found as urate anion in physiological pH. Urate is readily filtered by the glomerulus and reabsorbed by the proximal tubular cells of the kidney. 10% is the normal fractional excretion of uric acid in the body. The normal value of uric acid is 3.4 – 7.2 mg/dl in males and 2.4 – 6.1in females. Hyperuricemia is defined as increased levels of uric acids and its accumulation that occurs due to overproduction, underexcretion or both. Uric acid activates various inflammatory transcription factors and systemic cytokine production. When there is sepsis, elevated uric acid occurs due to cellular breakdown and many other mechanisms. Uric acid, having both oxidant and antioxidant properties, is found to play a role in these processes. Multiorgan failure in sepsis is due to great levels of oxyradicals and low levels of antioxidants. Henceforth measurement of uric acid can be used as a marker of oxidative stress in patients diagnosed to have sepsis.

MATERIAL AND METHODS

This study is carried out as a prospective cohort study in clinically assumed sepsis patients with age more than 18 years, in medical intensive care unit in Rama Medical College and Research Centre, Hapur from January 2022 till June 2022. Informed consent was booked for the study. A total no of 62 patients with clinical diagnosis of sepsis founded on the QSOFA criteria during the study period fulfilling the following inclusion criteria Inclusion criteria. All Patients admitted to medical intensive care unit with a clinical diagnosis of sepsis, age more than 18 years based on the QSOFA criteria. Exclusion criteria include all pregnant females, Patients from an outside facility, in medical intensive care unit for more than 24 hours. q SOFA score (also known as quick SOFA) is a score that may recognize patients with supposed infection who are at bigger risk for a poor outcome. It uses three criteria, assigning one point for low blood

pressure (SBP≤100 mmHg), high respiratory rate (≥22 breaths per min), or altered mentation (Glasgow coma scale <15). 2 or 3 points indicate high risk of poor outcome in patients with clinically suspected sepsis. Once the patient met the inclusion criteria blood samples were obtained for uric acid, urea, creatinine, complete blood count, arterial blood gas analysis, serum electrolytes and chest x ray was done. The primary end point was correlation between hyperuricemia in clinically suspected sepsis patients and morbidity and mortality rate. The secondary end points was correlation between hyperuricemia in clinically suspected sepsis patients and acute kidney injury, ARDS, duration of stay in hospital.

All statistical analysis was performed by SPSS software version 24. Descriptive statistics like mean and percentages were used for the analysis.

OBSERVATION AND RESULTS

Table 1: shows the correlation between hyperuricemia and the prolonged duration of stay in hospital. Among patients with hyperuricemia, 88.57 % required intensive care for more than 72 hours. 40.75% of patients with normal uric acid levels required intensive care stay for more than 72 hours. Majority of the hyperuricemic patients among sepsis study population had prolonged duration of stay in hospital which signifies increased morbidity. This data was statistically significant.

DURATION OF STAY, N= 62	URIC ACID ≥7mg/dl		URIC ACID<7 mg/dl		p VALUE
	NUMBER	%	NUMBER	%	
> 72 HOURS (N= 42)	31	88.57%	11	40.75%	0.000
≤ 72 HOURS (N= 20)	4	11.42%	16	62.96%	
TOTAL	35	100%	27	100%	

Table number 2 shows the correlate between hyperuricemia and the complications like AKI & ARDS. AKI was significantly higher in the hyperuricemia group. 66.66% of the septic patients with hyperuricemia developed AKI. Similarly, 72.72% of patients with hyperuricemia developed ARDS and both was significantly higher in the hyperuricemia group. 87.5% of the septic patients with hyperuricemia developed both. p value was found be statistically significant with a value of < 0.001.

COMPLICATION N= 62	URIC ACID ≥7mg/dl		URIC ACID<7 mg/dl		p VALUE
	NUMBER	%	NUMBER	%	
ACUTE KIDNEY INJURY (AKI) (N = 27)	18	40.0 %	09	33.33 %	0.001
ACUTE RESPIRATORY DISTRESS (ARDS) (N = 11)	08	17.14 %	03	11.11 %	
AKI & ARDS (N=8)	07	8.57 %	01	03.70 %	
NO COMPLICATION (N=16)	02	2.86 %	14	51.85 %	
TOTAL	35	100%	27	100%	

Table 3 shows hyperuricemia vs outcome one of the end points of this study is the outcome of patient's status with regards to sepsis and its relation to hyperuricemia. In this study, it was found that out of the 35 patients with hyperuricemia, 25 had died which 9 were discharged which is 28.1%. However, this was not statistically significant.

DURATION OF STAY, N= 62	URIC ACID ≥7mg/dl		URIC ACID<7 mg/dl		p VALUE
	NUMBER	%	NUMBER	%	
DEATH (N= 34)	25	71.43%	09	33.33%	0.192
DISCHARGED (N= 28)	10	28.57%	18	66.66%	
TOTAL	35	100%	27	100%	

DISCUSSION

The outcome of our research showed that patients with hyperuricaemia on coming to the emergency room were at greater risk of acute kidney injury, and the total prognosis including mortality rate was deprived in patients with hyperuricaemia . In a study by Akbar et al., the data on 144 patients admitted with sepsis was established to be linked with poor prognosis. The writers in the aforesaid study determined that patients with hyperuricaemia were more prone to an increased risk for acute kidney injury and ARDS. Our study is in cognisance to their results. The data on 237 patients from Korea discovered that patients with low serum uric acid had expressively better existence rate equated to those with hyperuricaemia, and the writers believed that serum uric acid can be employed as a prognostic marker in patients with ARDS. In alternative study, hyperuricaemia in the emergency department foretold the obligation of mechanical ventilation in a patient with sepsis. The results of our study are in line with this study the patients with higher uric acid levels had higher rates of respiratory failure.

CONCLUSION

We believe is that there was a lesser number of patients in the study; nevertheless, we believe that measurement of serum uric acid levels at the arrival of the patient predicts the severity of the illness in a given patient with sepsis.

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