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Estimation of Uric Acid Level for the Assessment of the Severity of Diseases with Clinically Diagnosed Sepsis

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Abstract

Background and Aim: The incidences of sepsis and septic shock depend on how acute organ dysfunction and infection are defined as well as on which data sources are studied. Hence this study was conducted to bring out the correlation between hyperuricemia in clinically diagnosed sepsis patients and morbidity and mortality.

Material and Methods: Total of 150 patients was included in the study. For the uric acid estimation of the included patients; blood samples were taken from the patient. For the biochemical estimation of the uric acid level the collaboration was done with the department of biochemistry, medical college and hospital.

Results: Among the 150 study participants, 64 patients had elevated uric acid levels which constitutes about 42.7%, whereas 86 patients constituting 57.3% had normal uric acid levels. It can be inferred that among the study population, patients had type 2 diabetes mellitus as the most common comorbidity at 40%. The most prevalent comorbidities among the patients with hyperuricemia were diabetesmellitus type 2 and type 1, decompensated liver disease and cerebrovascular accident. Patients without any comorbidities about 36% of the study population also developed sepsis.

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 IMCU. This study recommends further studies on a large basis to confirm the observations.

Keywords: Uric acid; sepsis; morbidity; serum level.

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INTRODUCTION

The incidences of sepsis and septic shock depend on how acute organ dysfunction and infection are defined as well as on which data sources are studied. Disparate estimates come from administrative data, prospective cohorts with manual case identification, and large electronic health-record databases.[1] Organ dysfunction is often defined by the provision of supportive

therapy, in which case epidemiological studies count the "treated," rather than the actual, incidence. In the United States, recent cohort studies using administrative data suggest that upwards of 2 million cases of sepsis occur annually.[2,3]

In the past 20 years, research has revealed that infection can cause multiple organ dysfunction but without a measurable inflammatory excess (i.e., without the systemic inflammatory response syndrome [SIRS]). In fact, both pro-and antiinflammatory responses are present along with significant changes in other pathways. Septic shock is defined as a complication of sepsis resulting in derangements in circulatory and metabolic pathways in the body Allantoin is the end product of purine metabolism in animals whereas uric acid in human beings.[4,5]

Purines can be endogenous or exogenous. Purines are nitrogenous compounds found in the body as well as food. Uric acid passes through the liver, enters the blood stream and most of it excreted in urine. Some uric acid is degraded in the body after reaction with oxidants.[6] Over the last ten years, strong association has been found between atherosclerosis, hypertension, hyperinsulinemia and chronic kidney disease and uric acid.[7]

Oxidative stress is found out by the presence of elevated serum uric acid which is a poor prognostic sign in case of patients with sepsis as multi organ dysfunction occurs as a result of high oxygen free radicals. Increased levels of serum uric acid causes acute activation of many transcription factors in patients with severe infection and is a poor prognostic sign in case of severe infection.8 Chronic conditions is also associated with elevated serum uric acid. Hence this study was conducted to bring out the correlation between hyperuricemia in clinically diagnosed sepsis patients and morbidity and mortality.

MATERIAL AND METHODS

The present prospective study was done in the medical college and the associated hospital. The study was done or the period of one year. Total of 150 patiens were included in the study. The inclusion and exclusion criteria followed were as follows:

Inclusion Criteria: 1. Age more than 18 years 2. Admission to IMCU with a working diagnosis of sepsis ***Exclusion Criteria***: 1. Patients denying consent 2. Pregnant females 3. Known case of kidney disease 4. Patients who have already been in IMCU in an outside facility for more than 24 hrs 5. Patients who are known case of gout 6. Patients on drugs causing hyperuricemia.

For the uric acid estimation of the included patients; blood samples were taken from the patient. For the biochemical estimation of the uric acid level the collobration was done with the department of biochemistry, medical college and hospital. The present study was conducted over a period of one year in the IMCU of Government Medical College and Hospital among 150 patients who were more than 18 years old and admitted in the IMCU with a clinical diagnosis of sepsis based on the quick SOFA (qSOFA) score.

Once the patient met the inclusion criteria, the written consent was signed and obtained from the study participants. Clinical proforma for the study including demography was meticulously collected from the study participants. Basic vitals at admission heart rate, respiratory rate, blood pressure, oxygen saturation were recorded.Thorough general and systemic examination performed. Quick SOFA score is based on three parameters; glassgow coma scale, systolic blood pressure and respiratory rate, assigning one point each to: 1. Low blood pressure SBP <= 100 mmHg, 2. High respiratory rate (>=22 breaths per minute) and 3. GCS < 15.

Blood samples were then obtained for uric acid, urea, creatinine, complete blood count, serum electrolytes and chest xray was taken. The patient's creatinine at admission to IMCU was taken as the baseline value. Hyperuricemia was defined as value more than 7 mg/dl in males and females. Outcome of the sepsis event was classified as either death or discharge from the intensive care unit.

RESULTS

In the present study population, the median age was found to be 59.13 years. There weer 6.67% who were under 30 years, 56% belonged to 30-65 years age group and contributed to the maximum number o individuals, followed by 37.33% in the ≥ 65years age group. Our study population had a slight male preponderance at 52%.

Uric Acid: Among the 150 study participants, 64 patients had elevated uric acid levels which constitutes about 42.7%, whereas 86 patients constituting 57.3% had normal uric acid levels. It can be inferred that among the study population, patients had type 2 diabetes mellitus as the most common comorbidity at 40%. The most prevalent comorbidities among the patients

with hyperuricemia were diabetesmellitus type 2 and type 1, decompensated liver disease and cerebrovascular accident. Patients without any comorbidities about 36% of the study population also developed sepsis.

The study participants were found to develop acute kidney injury, acute respiratory distress syndrome as the major complications. Our study aims at understanding the correlation between hyperuricemia and the secondary end points like AKI& ARDS. One of the end points of this study is the outcome of patients status with regards to sepsis and its relation to hyperuricemia. In this study, it was found that out of the 64 patients with hyperuricemia, 46 had expired which constitutes 71.9% and 18 patients were discharged which is 28.1%. However, this difference was found to be not statistically significant.

Table 1: Distribution of hyperuricemia among various age groups.

Age group	Frequency	Uric acid > 7 mg/dl	Uric acid < 7 mg/dl
< 30	10	4	6
31 – 65	84	36	48
> 65	56	24	32
Total	150	64	86

DISCUSSION

In this prospective cohort study, we report that elevated uric acid levels on arrival to the IMCU in patients with sepsis are associated with a poor prognosis; that is, an increased risk for AKI, ARDS, marks an increased duration of stay in the IMCU.

Sepsis is a condition of increased pro inflammatory cytokines and oxidative stress thereby increases the antioxidants in the body to counterbalance. This altered level of antioxidant defence leads to immune dysfunction and poor outcomes. In a systemic inflammatory response, both endothelial cells and neutrophils are activated to release oxygen-derived free radicals.[9,10]

Uric acid increases in response to acute oxidative stress. Uric acid formation may even provide a significant antioxidant defense mechanism against nitration by peroxynitrite in rat heart during hypoxia. Hence uric acid is believed to be an important marker of oxidative stress. The mechanisms for increased uric acid are not well understood.[11]

Development of AKI during sepsis increases patient morbidity, predicts higher mortality, has a significant effect on multiple organ functions, is associated with an increased length of stay in the intensive care unit, and hence consumes considerable healthcare resources. The first important finding of our study is that hyperuricemia is associated with AKI in patients with early sepsis. When AKI develops, then it causes poor prognosis. For instance, the immediate operative and postoperative death rate after CVS surgery ranges between 1 to 2%, this rises to 10 to 38% if AKI develops and to >50% if dialysis is needed.[12]

Usually the patients with sepsis are a very complex subset of population who have MODS and bad prognosis and are usually very sick patients. Hemodynamic changes, changes in the functional capacity of the heart and liver, exposure to multiple medications and numerous other factors cause development of AKI in these patients. Among these factors, uric acid can also contribute to development of AKI. The mechanism by which uric acid causes AKI can range from indirect injury secondary to the release of vasoactive mediators and oxidative stress to crystal induced direct tubular toxicity. Uric acid induced renal vasoconstriction due to catecholamine release, activation of renin-angiotensin system, release of pro-inflammatory markers, oxidative stress and decreased nitric oxide levels, in turn causes AKI.

Khosla et al. have revealed a decrease in plasma nitrites (metabolites of NO) in rats with hyperuricemia by allopurinol. Zoccali et al.[12] have demonstrated a correlation between high uric acid levels and dysfunction of endothelium . Various pro-inflammatory markers such as MCP and CRP are increased as a response to inflammation induced by uric acid.Uric acid stimulates an inflammatory response via increasing various pro-inflammatory markers such as MCP and CRP.[13,14]

Hence uric acid may be an early marker of impending AKI in patients with sepsis and could be used to predict the risk for AKI in septic patients. This further raises the question of whether the treatment of hyperuricemia in early sepsis could potentially decrease the risk for AKI. Increased uric acid levels play a role not only in the occurrence of AKI but also in the progression of CKD. Uric acid levels are increased in subjects with renal disease as the result of reduction in GFR and renal urate

excretion.

In our study we found that although there was a high incidence of ARDS noted in this septic patient population, there was no statistically significant association of hyperuricemia with ARDS. Thus although uric acid levels may be used to predict the severity of illness, duration of stay inIMCU, and risk for AKI, it was not significant enough to predict the incidence of ARDS.

This could potentially be due to the small patient population that we had for our study, especially since increasing uric acid levels have been reported by Nagaya et al. to correlate with clinical severity of primary pulmonary hypertension and has an independent association with long-term mortality of patient with primary pulmonary hypertension. This was most likely due to the small sample size.

Regarding the outcome of septic patients, though there was a slight increase in mortality among the hyperuricemic individuals with sepsis than those with normal Uric acid levels, it was statistically significant to prove the point. One statistically significant end point was the correlation between mechanical ventilation and ARDS and AKI. It was statistically significant to see increased mechanical ventilation among patients with ARDS.

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 IMCU. This study recommends further studies on a large basis to confirm the observations.

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