



Relationship Between Serum Level of Uric Acid and Out Come of Elderly Patients Admitted to Geriatric ICU with Systemic Infection on Admission

KEYWORDS

elderly, ICU, prognosis, serum uric acid, systemic infection

Dr. Somaia M. Ebeid

Associate professor of Geriatric Medicine and Gerontology, Faculty of medicine, Ain Shams University, Cairo, Egypt.

Dr. Nahla Fawzy Abou elezz

Associate professor, ocommunity, environment and occupational medicine, Faculty of medicine, Ain Shams University, Cairo, Egypt.

Dr. Heba Y. Kamel

Lecturer of Geriatric Medicine and Gerontology, Faculty of medicine, Ain Shams University, Cairo, Egypt.

ABSTRACT

Background : the debate about the role of serum uric acid as an anti-oxidant versus being a substance that exert oxidative stress upon the living cell in vivo which affect the prognosis of different illnesses including infectious diseases is an interesting issue for research.

Objective: of the current study was to evaluate the relationship between serum uric acid and prognosis of a group of elderly patients who had solitary or multiple sites of infections upon admission to geriatric ICU (Intensive Care Unit).

Methodology : forty four elderly patients , both males and females , sixty years old and above were recruited from the ICU of Geriatric department, Ain Shams university hospital. And they were divided into cases and control groups according to their serum uric acid on admission, they were subjected to history taking included: demographic data, SOFA score, site(s) of infection and prognosis upon discharge. then serum uric acid , serum creatinin and BUN(Blood Urea Nitrogen) were measured within 24 hours of admission

Results: among the participants the median serum level of uric acid was 7.235 ± 2.95 with no statistically significant correlation between it and the socio-demographic and clinical data of the patients, but there was statistically significant correlation between it and prognosis of the patients while sofa score not. By ANOVA test only serum uric acid and creatinin showed statistically significant correlation with the prognosis while age, gender and serum BUN didn't.

Conclusion & Recommendation: uric acid is an important prognostic factor for ICU elderly patients and should be investigated more whether to be routine investigation or not for this group of patients.

Introduction:

Uric acid is an end product of the metabolism of purine through the action of xanthine dehydrogenase or xanthine oxidase. It is present in blood and is excreted in the urine. Normal levels of blood uric acid range from 0.09 to 0.42 mmol/L in adults, with slightly higher values for elderly patients. It is well established that oxidative stress is involved in a spectrum of acute and chronic pathologies, including cardiovascular, neurodegenerative, inflammatory, neoplastic and infectious diseases[1-4]. Moreover, oxidative stress plays a key role in aging [5].

Critical illnesses, such as sepsis or acute lung injury (ALI) acute respiratory distress syndrome(ARDS), are characterized by a severe production of reactive oxygen species (ROS) and other radical species with consequent oxidative stress [6].

The immune cell functions are specially linked to ROS generation, such as that involved in the microbicidal activity of phagocytes, cytotoxic activity or the lymphoproliferative response to mitogens [7]. However, excessive amounts of ROS are harmful for the immune cells, because they can attack cellular components and lead to cell damage or death by oxidizing the membrane lipids, protein, carbohydrates and nucleic acids. To prevent these effects of ROS, they can be neutralized by the complex anti-oxidant system that the organisms have developed [2]. Thus, anti-oxidants play a vital role in maintaining immune cells in a reduced environment and in protecting them from oxidative stress [8].

Uric acid's antioxidant activities are also complex. And

there is a debate about its oxidant-anti-oxidant activity when its serum level is low or high, supposing that it acquires oxidant stress effect in high level.

By studying its antioxidant properties it was found that:

UA(Uric Acid) has the highest concentration of any blood antioxidant.[9] and provides over half of the total antioxidant capacity of human serum.[10]

It has been suggested that Serum UA could be a marker of oxidative damage [11]

As an indicator for evaluating the oxidation-antioxidation status of organisms, uric acid possesses protective effect on vitamin C [12]. And as an endogenous aqueous antioxidant in humans it contributes as much as 2/3rd of all free radical scavenging capacity in plasma [13].

Elderly patients in the intensive care unit usually have experienced a variety of pathogenic courses such as ischemia-reperfusion injury, inflammation and dysfunction of blood coagulation which uric acid may be a factor involved in the above mentioned pathogenic courses, and may have potential value for the assessment of changes in clinical settings and prognosis of illness[14], in addition to its previously mentioned role in the process of physiological aging.

So AIM of the current study was carried out to evaluate the relationship between serum uric acid in ICU elderly patients and their outcome in respect of prognosis of infection .

Patients and Method:

Study design:

A case - control study

Setting:

the participants were recruited from Elderly ICU of geriatric department, Eldemerdash hospital. Ain Shams University

Subjects

forty four elderly 60 years and older, both males & females and they were divided into two groups:

Cases : 22 elderly patients with hyperuricemia**Controls : 22 elderly patients with normal serum uric acid**

Both groups were admitted to the Geriatric ICU with solitary or multiple sites of infection diagnosed upon admission or during hospital stay.

Methodology:**All subjects were subjected to the following:**

1-An oral consent to participate in the study was taken

2-history taking which included:

I-demographic data: Name ,age ,gender .

II- period of ICU (intensive care unit) admission

III- period of hospital stay

IV - diagnosis on admission

V - comorbid conditions

VI - SOFA score

VII- Regarding infection : number, site and type

VIII-prognosis of infection :

Died, remained unchanged, improved, completely healed

The inclusion criteria of patients were those with solitary or multiple sites of infection diagnosed within 24 hours of admission.

3-Laboratory investigation:

-serum levels of uric acid,

-creatinine and blood urea nitrogen (BUN)

Both were detected within 24 hours after admission.

Statistical analysis :

- Quantitative data e.g. age are presented as mean \pm standard deviation. Independent t test is used to compare such data between two groups and one-way ANOVA is used when more than two groups are to be compared.

- Qualitative data e.g. sex, are presented as count and percentage. Chi-squared test is used to compare such data between two or more groups.

- The r^2 value represents the proportion of variation of the dependent variable that is predicted from the independent variable. An r^2 of 1.0 indicates that all the plotted points lie on a straight line and that the dependent variable can be predicted from the independent variable with 100%.

Ethics :

The study was approved by the scientific board of Geriatrics and Gerontology department, faculty of medicine Ain Shams University.

Result & discussion:**Demographic and clinical data :**

Among the patients, 23(47.92%) were male and 25(52.08%) were female, with a mean age of 68.00 ± 7.95 years (median 65 years). 83.3% were young old, 12.5% were old and 4.2% was among the oldest

group.

Twenty eight (58.3%) of the participants had got one site of infection, 16(33.3%) with two sites of infection and four(8.3%) with 3 sites of infections.

The most common associated comorbid conditions were hypertension and diabetes mellitus that each was found in 52.1% among the participants as shown in **table (1)**

The average hospital stay was 6.75 ± 4.25 days (median 6 days). Average sofa score was 4.98 ± 2.83 (median 4).

Within 24 hours after admission, the major relevant laboratory results were as follows: uric acid was 7.235 ± 2.95 (median=7.2), serum creatinine was 1.875 ± 1.74

With (median 1.2), and blood urea nitrogen was 45.90 ± 25.99 with (median = 39).

Regarding prognosis, seven patients representing 14.6% of the participants completely recovered, sixteen patients representing 33.3%, five patients representing 10.4%, and 20 died representing 41.7%.

Correlation between uric acid level and sociodemographic data:

- With **Gender**, mean serum uric acid among the males participants was 7.278 while among females participants was 7.196 but no statistically significant difference ($p = 0.92$). And this agrees with [15]. Also agrees with the general concept that women have far lower prevalence of gout compared to men and this gender difference gets smaller with increasing age, but men still far outnumber women with gout, even among the elderly [14].

- There was no statistically significant correlation between age of the participants and serum uric acid (**table 2&3**). And this disagrees with [16], who concluded that SUA levels in men and women increased with advancing age, but this may be explained by the difference of the studied age group in both studies, that [16] Kuzuya M1, Ando F, et al compared elderly group with younger ones with an average age of 44.5 years for the men and 43.7 years for the women, while in the current study a mean age of 68.00 ± 7.95 years.

- By using Student t test there was no statistically significant correlation between mean value of serum uric acid and any of the associated comorbid conditions as regard: coronary heart disease the current study ($t = -1.1$, $P = 0.29$), neoplasm ($t = -0.78$, $P = 0.43$), hypertension ($t = -1.4$, $P = 0.17$), diabetes mellitus ($t = -1.6$, $P = 0.12$), and cerebral infarction ($t = -0.39$, $P = 0.69$) this agrees with [15] as regard IHD and neoplasm and disagrees as regard hypertension and diabetes mellitus.

- Also in the current study there was no statistically significant association between uric acid and: COPD ($t = -0.32$, $P = 0.75$), CHF ($t = -1.5$, $P = 0.12$), Bronchial asthma ($t = -1.17$, $P = 0.26$), cor pulmonale ($t = -0.9$, $P = 0.36$), and anemia ($t = -0.53$, $P = 0.59$)

- The present study showed a linear correlation between serum uric acid and BUN ($r^2 = 0.39$, $P = 0.006$) and creatinine ($r^2 = 0.16$, $P = 0.29$), Figure (1&2) and this reflects the affection of the serum level of uric acid was by many factors such as protein metabolism and renal function, this agrees with [15], who found the same result.

Correlates of prognosis:

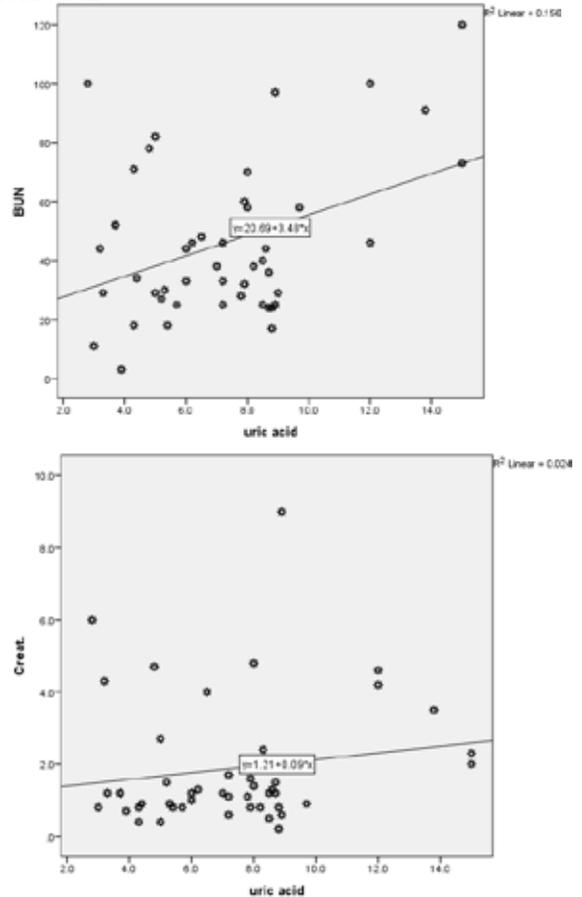
- There was no statistically significant correlation between serum uric acid and sofa score of the

patients(table 4)

- By using ANOVA test to assess the correlation between sofa score and prognosis versus that of mean serum uric acid and prognosis , it was found that there was no statistically significant correlation between sofa score and prognosis, while there was highly statistically significant correlation between mean serum uric acid and prognosis,(table 5) this agree with the results of [15] who usedAPACHEII score & not sofa as in our current study . And this result also support our hypothesis that uric acid is an emerging prognostic factor among ICU elderly patients in contrast to the current used ones.
- Age, gender and BUN had no statistically significant correlation with prognosis pvalues respectively(p= 0.45), p=0.39 and (p= 0.1). while s. creatinin show statistically significant correlation(p= 0.05). while serum uric acid show highly statistically significant correlation(p= 0.002). (table 6&7)
- Regarding the associated comorbid conditions there was no statistically significant correlation with prognosis as follow:-hypertension (p value=0.34), diabetes mellitus(p value=0.68),IHD(p value=0.53),COPD(p value=0.94), chronic liver disease(p value0.19), CHF(pvalue=0.95), bronchial asthma(pvalue=0.82), malignancy(pvalue=0.68), old CVS(pvalue=0.24) and anemia(pvalue=0.69).
- These result indicate that serum uric acid is a strong predictor of morbidity and mortality among ICU elderly patients regardless other known ones as age, gender,underlying comorbid conditions and lab. Values as BUN.

young old 60 - 74 years	40	7.283	2.7437	F=0.113 p=0.89
old old 75 - 84 years	6	7.250	4.4912	
≥85 years	2	6.250	3.3234	
Total	48	7.235	2.9446	

Figue(1&2):



Tables :

Table (1): Associated comorbid conditions:

Co-morbidity		
1-HTN	25	52.1
2-DM	25	52.1
3-IHD	10	20.8
4-COPD	2	4.2
5-CLD	5	10.4
6-CHF	2	4.2
7-B.A.	3	6.3
8-ARRHYTHMIA	0	0
9-BUDD CHIAR\$	1	2.1
10-MALIGNANCY	4	8.3
11-OLD C.V.S.	2	4.2
12-HEARING .I.	1	2.1
13-PROSTATE ENLARGEMENT	1	2.1
14-COREPULMONALE	2	4.2
15-ANEMIA	1	2.1

Table (2&3)

Correlation between age and uric acid level

	Mean	Std. Deviation	Sig.
Age N=48	68.00	7.952	r= -0.04
uric acid N=48	7.235	2.9446	p=0.74

Relation between age groups and uric acid level

	N	Mean	Std. Deviation	Sig.
--	---	------	----------------	------

Table(4): Correlation between uric acid and sofa score

	Mean	Std. Deviation	Sig.°
sofa score	4.98	2.832	r= 0.076 p=0.607
uric acid	7.235	2.9446	

° Pearson correlation r²

Table(5): Relation between sofa score and uric acid with prognosis

Prognosis	N	Mean	Std. Deviation	Sig.	
sofa score	complete resolution	2	6.00	1.414	F= 1.360 P= 0.267
	partial resolution	21	4.19	2.136	
	Deterioration	5	4.40	2.966	
	Death	20	5.85	3.376	
	Total	48	4.98	2.832	

uric acid	complete resolution	2	3.700	.9899	F= 5.880 P= 0.002
	partial resolution	21	5.871	2.5203	
	Deterioration	5	9.160	1.6334	
	Death	20	8.540	2.8304	
	Total	48	7.235	2.9446	

ANOVA test

Table (6) Relation between uric acid and socio-demographic and clinical data with prognosis ANOVA test

Prognosis		N	Mean	S.D	Sig*
Age	complete resolution	2	76.00	0.0	F= 0.91 p= 0.45
	partial resolution	21	66.76	7.76	
	Deterioration	5	67.20	6.46	
	Death	20	68.70	8.67	
uric acid	complete resolution	2	3.700	0.99	F= 5.8 p= 0.002
	partial resolution	21	5.871	2.52	
	Deterioration	5	9.160	1.63	
	Death	20	8.540	2.83	
BUN	complete resolution	2	22.50	16.26	F= 2.2 p= 0.1
	partial resolution	21	38.14	18.13	
	Deterioration	5	52.60	26.05	
	Death	20	54.70	30.84	
Creat	complete resolution	2	.850	0.071	F= 2.77 p= 0.05
	partial resolution	21	1.424	1.11	
	Deterioration	5	3.660	3.31	
	Death	20	2.005	1.64	

Table (7)Relation between Gender and prognosis

Prognosis	Gender	
	Female	Male
	No (%)	No (%)
complete resolution	0 (0.0)	2 (8.7)
partial resolution	11 (44.0)	10 (43.5)
Deterioration	2 (8.0)	3 (13.0)
Death	12 (48.0)	8 (34.8)
Total	25 (100.0)	23 (100.0)

$\chi^2 = 2.97$ p=0.39

Conclusion and Recommendations :

Results of the current study showed that serum uric acid was more statistically significant than other prognostic factors as age , gender and more than sofa score in predicting prognosis of elderly patients admitted to ICU with systemic infection. Thus it is an emerging prognostic factor which does worth more studies to confirm being essential routin tests for these patients.

Contributions

Dr.Somaia Mohamed Ebeid (associate professor of Geriatric medicine)

- concept of the study.
- design of the study.
- collection of data.
- analysis and interpretation of the results.
- preparation of the manuscript.
- revesion_of the manuscript_.

Dr. Nahla Fawzy abouelezz(associate professor of Community medicine)

- design of the study.
- statistical analysis.
- analysis and interpretation of the results.

Dr.Heba Youssef Kamel(lecturer of Geriatric medicine)

- collection of data.

Disclosure statement:

No potential conflicts of interest were disclosed.

REFERENCE

1. Halliwell, B. and Gutteridge, J.M. (1989): Free radicals in biology and medicine. Clarendon Press, Oxford. 2.Van Lenten, B.J.,et al(2001): The role of high-density lipoproteins in oxidation and inflammation. Trends in Cardiovascular Medicine, 11, 155-161. 3.Stocker, R. and Keaney Jr., J.F. (2004): Role of oxidative modifications in atherosclerosis. Trends in Cardiovascular Medicine, 84, 1381-1478. 4.Barnham, K.J., Masters, C.L. and Bush, A.I. (2004): Neurodegenerative diseases and oxidative stress. Nature Reviews Drug Discovery, 3, 205-214. 5.Floyd, R.A. and Hensley, K. (2002): Oxidative stress in brain aging. Implications for therapeutics of neurodegenerative diseases. Neurobiology of Aging, 23, 795-807. 6.Gutteridge, J. M.; Mitchell, J.(1999): Redox imbalance in the critically ill. Br. Med. Bull. 55:49- 75; 1999. 7.Goldstone SD and Hunt NH.(1997) :Redox regulation of the mitogen- activated protein kinase pathway during lymphocyte activation. Biochim. Biophys. Acta 1997; 1355: 353-60. 8-McArthur WP. :Effect of aging on immunocompetent and inflammatory cells. Periodontol. 2000 1998; 16: 53-79. | PubMed | ChemPort | 9- Glantzounis G. K. et al (2005): "Uric Acid and Oxidative Stress". Current Pharmaceutical Design 11 (32): 4145-51. 10- Becker, B (1993):"Towards the physiological function of uric acid". Free Radical Biology and Medicine 14 (6): 615-31. 11. Tamariz L, et al.(2011): Association of serum uric acid with incident atrial fibrillation (from the atherosclerosis risk in communities [ARIC] study. Am J Cardiol., 2011; 108(9):1272-1276 12. Batra S, et al. (2000): Alterations in antioxidant status during neonatal sepsis. Ann Trop Paediatr. 2000;20:27-33. [PubMed] 13. Squadrito GL,et al.(2000):Reaction of Uric Acid with peroxy nitrite and implications for the mechanism of neuroprotection by uric acid. Arch Biochem Biophys 2000; 376:333-7. 14- Jasvinder A.(2013):Racial and Gender Disparities in Patients with Gout.Curr Rheumatol Rep.2013Feb;15(2):307. 15-He-chen Zhu and Ruo-lan Cao (2012): the relationship between serum level of uric acid and prognosis of infection in critically ill patients. World J Emerg Med, 2012;3(3):186-190 . 16- Kuzuya M1, Ando F, Iguchi A and Shimokata H.: Effect of aging on serum uric acid levels: longitudinal changes in a large Japanese population group. J Gerontol A Biol Sci Med Sci. 2002 Oct;57(10):M660-4