



## VALUE OF BLOOD LACTATE AND TSH IN PREDICTING LENGTH OF HOSPITALIZATION AND OUTCOME OF POISONED PATIENTS ADMITTED TO THE ICU

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### ABSTRACT

Objective: There is evidence that measuring levels of endocrine hormones, lactate and Simplified Acute Physiology Score II (SAPSII), can predict the prognosis and length of hospitalization of a poisoned patient. This study was conducted to evaluate levels of TSH hormone and serum lactate among poisoned patients admitted to the ICU during one year. Methods: In this cross-sectional study, patients who were admitted to the Toxicology ICU were non-randomly enrolled in the study after consent forms were obtained from the closest relatives. After sampling, serum levels of TSH and lactate were measured using similar kits. Data were analyzed by SPSS software (version 21). Results in this descriptive cross-sectional study, total of 150 patients with an average age of 39 years were examined, and 26 patients died. Simplified Acute Physiology Score II (SAPSII) and lactate were identified as prognostic factors for disease outcome. Moreover, after adjusting age and gender using Logistic Regression analysis, chance of death among patients was increased by 10% with the addition of each one score to Simplified Acute Physiology Score II (SAPSII) (P value <0.01). Conclusion: Upon admission, serum lactate and Simplified Acute Physiology Score II (SAPSII) scoring system can help predict the outcome of poisoning in poisoned patients and play an important role in treatment and isolation of high risk patients. However, TSH cannot be considered as a prognostic factor. Further studies are recommended to certainly approve this conclusion Serum Lactate, TSH, Poisoning, ICU, prognosis.

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### Introduction

During critical illness, hormone levels alternate, and these alternations are correlated with morbidity and outcomes of patients in ICUs. To date, several studies with conflicting results have been performed with regard to thyroid hormone disorders and their impact on the recovery of patients hospitalized in the ICU. Studies have shown that in patients admitted to the ICU, several syndromes such as euthyroid sick syndrome or non-thyroidal illness syndrome (NTIS) impairs thyroid hormones [1]. These thyroid independent effects might result from inflammatory cytokines, which are released during the process of a disease and its subsequent acute conditions [2], but there are few studies about poisoned patients. Furthermore, measurement of serum lactate is one of the criteria in assessing the treatment process of drug poisoning. In several studies, lactate level of 2mmol/L is considered as the cutoff grade in anticipation of recovery [3]. Causative mechanisms of hyperlactatemia are beyond a particular drug overdose [4] and can be due to hypoperfusion following vasoconstriction associated with ergotamine use [5]; hypotension following to beta-blockers intake [6]; muscle activity due to cocaine-induced seizures [7]; myoclonus in serotonin syndrome [8]; changes in lactate metabolism and its production e.g. increased consumption of propylene glycol [9] or reduced clearance of lactate in metformin use [10]; duration of decreased level of consciousness [11]; mitochondrial DNA changes induced by nucleoside inhibitors [12]; defect in cellular respiration due to glycolysis in toxicity with acetaminophen and arsenic [13, 14]; Krebs cycle defects following monofluoroacetate [15]; defects in electron transport due to carbon monoxide and

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cyanide poisoning [16, 17]; uncoupling of oxidative phosphorylation in salicylism [18]; and finally due to etiologies such as septic shock, seizure, infection, and organ failure in trauma [19-22].

Maldonado et al. (1992) concluded that not only thyroid dysfunction in critically ill patients can determine the patient's prognosis, but also the hormonal changes have a direct correlation with disease prognosis [16].

Scores obtained from Simplified Acute Physiology Score II (SAPSII) have resulted from routine physiological measurements 24 hours after admission, patient's history, and other information obtained during hospitalization. Parameters include age (for patients older than 15 years old), heart rate, systolic blood pressure, body temperature, GCS, mechanical ventilation, arterial oxygen pressure or PaO<sub>2</sub>, the percentage of inspiratory oxygen or FiO<sub>2</sub>, urine output, BUN, sodium, potassium, bicarbonate, white blood cells count, history of chronic diseases, and type of admission. Afterwards, mortality rate is predicted by scoring between 0 and 163, and from 0 to 100%, [23]., the implementation of this research can result in targeted treatment in order to reduce patients' length of stay in the ICU.

### Methods of Research

This descriptive cross-sectional study was performed using non-random, convenience sampling. The standard sample size of 130 was calculated based on the Cohen's formula. To increase the level of validity, a total of 150 poisoned patients, who were admitted to the ICU of Imam Reza Hospital from 2014 until 2015, were enrolled in the study based on the inclusion criteria. Sampling was consecutive. Inclusion criteria were: 1) confirmed poisoning 2) consent to participate in the research 3) age more than 15 years 4) absence of any previous disease. Consent forms were obtained from the closest relatives of patients. Poisoning proof was done through the qualitative lab tests. The study protocol was approved by the ethical committee in treatment before hospitalization, and all medical records, physical examinations, and interview patients remained confidential. The exclusion criteria were as follows: 1) existence of any previous disease, 2) Pregnant women and those who were under treatment with hormones, 3) history of hospitalization or ICU admission during the last six months, 4) history of receiving radioactive iodine, 5) age below 15 years, 6) unknown poisoning.

Subsequently in all patients, venous samples of thyroid stimulating hormone (TSH) and serum lactate level were collected. The samples measured using similar diagnostic kits (thyroid-stimulating hormone with normal range of 0.4-5 mIU /L, and lactate with normal range: 0.01-2 mmol / L). Data were collected in self-designed data collection forms and analyzed by Logistic Regression and T-Test using SPSS software (version 21).

Ethical Considerations: Consent forms were obtained from the closest relatives of patients and complete consent form that confirmation by ethical committee in treatment vice chancellor, before hospitalization while all achieved data due to the medical records, physical examination, and interview patients will be remained confidential.

### Results

In this study of 150 patients, 105 patients (70 %) were men and 45 patients (30 %) were female. A total of 26 patients died (17.3 %) of which 19 patients (72 %) were male. Mean and standard deviation was calculated  $39.83 \pm 17.52$  for all patients which according to the gender were  $36.14 \pm 17.34$  and  $41.92 \pm 17.32$  in women and men respectively (Diagram 1). The ratio of men to women in both groups of survivors and deceased had no significant difference ( $P > 0.6$ ). In general, the mean age of the all patients was  $39.83 \pm 17.52$  years,  $36 \pm 13$  in survivors and  $50 \pm 21$  in dead patients. The difference between the two groups was statistically significant ( $p < 0.001$ ).

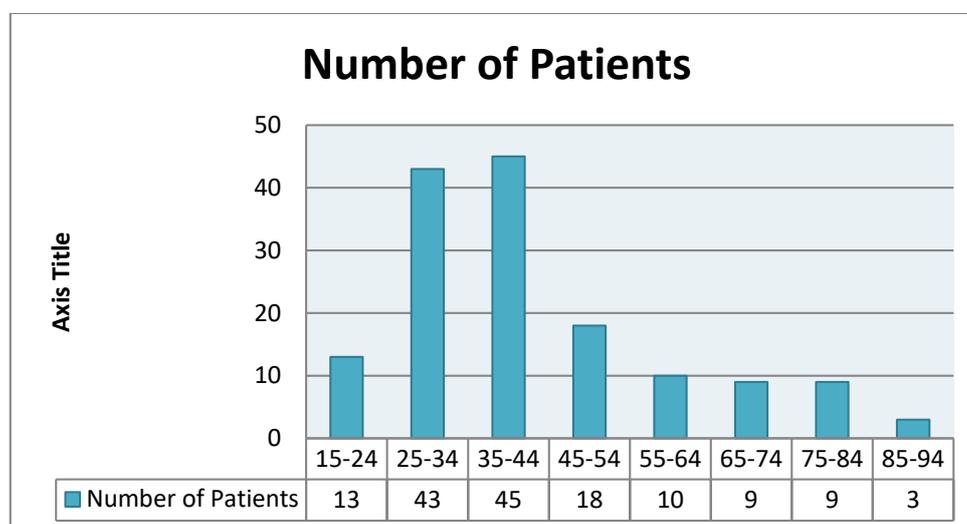


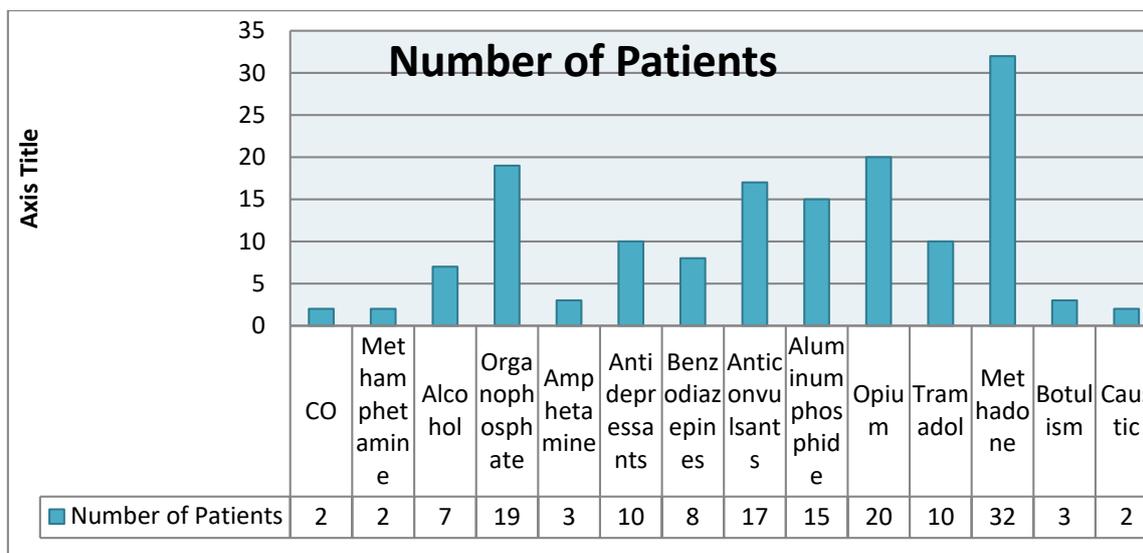
Diagram 1. Age distribution in poisoned patients hospitalized in ICU at Emam-Reza hospital in Mashhad

The most common types of poisoning in patients were as follows: opium (42.7%), sedatives (23.3%). (Table 1 & Diagram 2) The amount of consumption and poisoning dose was not significantly different between the deceased and the survivors ( $p>0.05$ ). The mean Simplified Acute Physiology Score II (SAPSII)  $\pm$  (SD) showed a significant difference between survivors ( $27.3\pm 7.8$ ) and deceased ( $36.6\pm 5.3$ ) patients ( $p<0.001$ ). Mean systolic and diastolic blood pressure showed no significant difference between the survivors and deceased patients ( $p>0.05$ ). The average level of lactate showed a significant difference between the two groups so that it was higher in deceased patients ( $6.5\pm 3.1$ ) compared to the survivors ( $1.3\pm 1$ ) ( $p=0.001$ ).

**Table 1.** Sex distribution in poisoned patients hospitalized in ICU at Emam-Reza hospital in Mashhad

Type of Poisoning	Number of Men %	Number of Women %	Total number
Organophosphate	7 (7.6%)	12(20.7%)	19 (12.7%)
Carbon monoxide	1 (1.1%)	( 1.7%)1	2 (1.3%)
Alcohol	7 (7.6%)	0(0%)	7 (4.7%)
methamphetamin	2 (2.1%)	1 (1.7%)	3 (2%)
Botulism	2 (2.1%)	1 (1.7%)	3 (2%)
Opioids	45 (48.9%)	19 (32.8%)	64 (42.7%)
Caustic	1 (1.1%)	1 (1.7%)	2 (1.3%)
Aluminum phosphide	8 (8.7%)	7 (12%)	15 (10%)
Sedative drugs	19(20.8%)	16 (27.7%)	35 (23.3%)
Total	92 (100%)	58 (100%)	150 (100%)

In addition, the comparison between the two groups of survivors and deceased with lactate level above 2 mmol/L showed that 50 patients in survivors group (40%) and 26 patients in deceased group (72%) had an elevate lactate ( $>2$  mmol/L) which this difference between the two groups was statistically significant ( $p<0.01$ ). The TSH mean  $\pm$ SD was  $1.9\pm 1.5$  and  $1.3\pm 1.2$  in deceased and survivors groups respectively, which this difference was not statistically significant ( $p>0.03$ ). The length of stay in ICU showed a significant difference between the survivors ( $6\pm 4$  days) and deceased ( $19\pm 10$  days) patients ( $p<0.001$ )



**Diagram 2.** distribution of ICU patients based on the type of poisoning in poisoned patients hospitalized in ICU at Emam-Reza hospital in Mashhad

Logistic regression analysis (raw) showed that Simplified Acute Physiology Score II (SAPSII) can be a prognostic factor for the indication of disease outcome (OR=1.10, 95% C. I=1.04-1.64 and P value=0.00). Moreover, the risk of death in these patients, with adjusted age and gender, increased by 10% for each additional point of Simplified Acute Physiology Score II (SAPSII) ( $p=0.02$ ). Logistic regression analysis (raw) also revealed that lactate level can be a prognostic factor for the disease outcome (OR= 1.2, 95% C. I=1.05-1. 44, P value=0.007). Besides, Logistic regression analysis (adjusted age and gender) showed that by the addition of each point to lactate, the chance of death increased by 13% in poisoned patients ( $p=0.004$ ). However, the Logistic regression analysis of TSH for both raw and adjusted data showed no significant difference; therefore, TSH cannot be considered as a prognostic factor ( $p>0.05$ ). Also, there was no significant correlation between Simplified Acute Physiology Score II (SAPSII) and lactate in the deceased group (Correlation Coefficient=0.0103 and P= 0.65) as well as survivors' group (Correlation Coefficient= 0.022 and P= 0.83).

## Discussion

In this study, the mean±SD age of all patients was 39.83±17.52, survivors 36±13 and deceased patients was 50±21 which this result showed an increase in the age of hospitalized and poisoned patients compared to the previous studies [22-26]. In a study by Talaei (2015) on different types of poisoning, the mean age of the patients was reported 36.6 years [27] while in the study by Hosseinian in Iran (2007-2008), the mean age of the patients was lower [28].

In this study, the serum lactate and Simplified Acute Physiology Score II (SAPS II) were indicated as mortality prognostic factors in poisoned patients admitted to the ICU. The result showed that by the addition of each point to Simplified Acute Physiology Score II (SAPS II) the risk of dead increased by 12%. The results of the study by Shadnia et al. (2010), which was carried out on 39 patients with acute aluminum phosphide poisoning and 24 patients with organophosphate poisoning, revealed that the calculation of Simplified Acute Physiology Score II (SAPS II) in the first 24 hours (score above 11) can be a good prognostic indicator in patients with acute poisoning with aluminum phosphide and organophosphate admitted to ICU [29, 30].

In the present study, Simplified Acute Physiology Score II (SAPS II) in both deceased and survivors' groups was 36.6±5.3 and 27.3±7.8 respectively ( $p<0.001$ ). What is of concern in this study is that the average Simplified Acute Physiology Score II (SAPS II) in survivors' group was also higher than 26. Furthermore, this study encompassed all kinds of poisoning, hence Simplified Acute Physiology Score II (SAPS II) results in both groups was higher than the previous study. This study also showed that after adjusting the age and gender, with each increase in serum lactate levels the mortality rate in poisoned patients increased by 15%. Reviewing 200 patients admitted to the ICU in 1993 and 1995, Rothwell assumed that high prevalence of abnormal levels of thyroid stimulating hormone (TSH) in those patients could be due to eutyroidism, and therefore, predicted the prognosis of the patients. It was found that the endocrine system disorder in patients had a prognostic value higher than APACHE II [18], and TSH>5 with the normal range of 0.4-5 was considered as the cutoff point in the study [17, 18].

In a retrospective study by Manini (2010), in which 150 patients were divided into two groups of subject and control, the results showed that serum lactate was significantly higher in patients with drug overdose effects upon admission to the emergency department [19]. Mégarbane studied patients with beta-blocker poisoning and showed that in mild poisonings, serum lactate level can be effective in anticipation of treatment process, while in severe poisonings lactate level alone cannot be used as an indicator of complications and treatment process [20]. Rothwell in 1993 and 1995 with a review of 200 patients admitted to the ICU determined that high prevalence of abnormal levels of thyroid stimulating hormone (TSH) in these patients assumed to be due to the eutyroidism, and on this basis predicted the prognosis in these patients. It was found that the endocrine system disorder in patients has prognostic value higher than APACHE II (18). TSH>5 with the normal range of 0.4-5 was considered as cutoff point in this study [17, 18].

The results of a study by Rishu et al on critical ill patients with the normal range of lactate (0.01-2 mmol/L) indicated that lactate level of 1.35 mmol/L is the best threshold which helps to distinguish the survivors from non-survivors. A considerable percentage of critical ill patients (47.5%), that their lactate were measured within 24 h after admission in ICU, had equal or lower than 2mmol/L serum lactate and mortality rate of these patients was 30% [25].

In this study, 41% of survivors versus 72% of deceased had lactate levels higher than 2mmol/L that the difference between the two groups was significant ( $P<0.002$ ). On the other hand, in 81 patients (54%) lactate levels were less than or equal 2 mmol/L and overall mortality rate was 17.3%. Trzeciak et al showed that the rate of dead in patients with infections is 15% in patients with the serum lactate level lower than 2mmol/L, 25% with lactate level 2.1-3.9 mmol/L and 38% in patients with lactate level higher than 4mmol/L ( $p<0.001$ ). [30] Despite the positive studies on changes in endocrine hormones, including TSH hormone and its prognosis value in patients, in this study the initial TSH levels in patients with different kinds of poisoning was not a significant prognostic factor.

## Conclusion

This study showed that lactate measurement and Simplified Acute Physiology Score II (SAPSII) scoring system in the poisoned patients at the time of admission not only can help to predict the outcome of poisoning but also can play an important role in the management of treatment and isolation of patients at higher-risk, while TSH measurement in these patients cannot be considered as a prognostic factor. Nevertheless, the further studies to confirm the validity of this conclusion are recommended. and preventive agent of complications, so that seizures and possibly death could be prevented.

**Advances in knowledge:** In the current study, serum levels of TSH cannot be considered as a prognostic factor in poisoned patient admitted to the ICU.

There was no significant correlation between Simplified Acute Physiology Score II (SAPSII) and lactate.

**Application to patient care:** The findings of the current study indicate that serum lactate and Simplified Acute Physiology Score II (SAPSII) scoring system can help predict the outcome of poisoning in poisoned patients and play an important role in treatment and isolation of high risk patients.

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