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The Association between Serum Lactate Level and Hospital Outcome in Children with Multi-Trauma

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Abstract

Background: Trauma is an important cause of disability and death in young people. This study aimed to investigate the association between serum lactate level and in-hospital mortality in multi-traumatic children.

Method: In this cross-sectional study, all children with multi-trauma admitted to the emergency department in Shohada and Imam Reza hospitals of Tabriz/Iran were evaluated from 2018 to 2020. At the time of admission to the emergency department, serum lactate, PRISM (Pediatric risk of mortality) score, and other findings as well as outcome were checked and correlated with the outcomes for all patients. Patients were classified into two groups (based on outcome) and six groups (based on lactate levels) to evaluate associations between results. The Chi-square test, independent samples t-test, ANOVA, and multivariate logistic regression test were performed in SPSS.22. P-value<0.05 and OR with 95% confidence interval were considered statistically significant.

Result: Out of 110 admitted children, 10 (9%) died in hospital. Mean lactate level was 3.2 mmol/l and 85 patients (77.2%) had lactate level>2 mmol/l (millimoles). The initial blood lactate level was directly correlated with mortality. This relationship was confirmed even after adjusting for variables such as the PRISM score (OR = 1.27; 95% CI, 1.19-1.35; P <0.001). Multiple regression study showed that a high lactate level (OR =1.17; 95% CI, 1.07-1.29; P=0.001), high PRISM score (OR = 1.15; 95% CI, 1.11-1.20; P<0.001), and low albumin level (OR =0.92; 95% CI, 0.88-0.96; P<0.001) were independent risk factors for mortality.

Conclusion: High blood lactate level was an independent factor in the increase of mortality rate in the emergency department.

Key Words: Association, Hospital mortality, Lactate, Multi-traumatic children, Pediatrics, Trauma.

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1- INTRODUCTION

Trauma refers to any type of stroke, injury, shock, or accident to the human body, if it impacts from the outside; and the internal agents and diseases in the body are not the cause of the injury (1). Trauma is the leading cause of death and one of the main causes of disability and active population in developing countries (2). Therefore, the diagnosis of the severity and extent of involvement in these patients are becoming more and more important (3) and it is necessary to conduct investigations for finding easier indexes for appropriate diagnostic and therapeutic procedures (4).

Management of patients with trauma starts from the pre-hospital environment and continues in the emergency and intensive care units (5, 6). With proper management, patients who suffer from multi-trauma or critical illnesses and are at higher risks of death, are to be under timely and appropriate treatments to prevent subsequent deaths and disabilities (7).

Although mortality in the traumatic patients is more dependent on the kind and severity of the injury (8), the evaluation of tissue hypoxemia, focus on airway management, and maintenance of arterial blood pressure could lead to improved physical conditions (9, 10). The measurement of vital signs is the first step in the initial assessment of patients 'condition and examination of patients' hemodynamic status. Other measurements, including oxygen saturation, have better accuracy and validity than vital signs (11).

Serum lactate is a marker of tissue hypoperfusion and cellular hypoxia (12). Insufficient oxygen supply to tissues is associated with increased lactate production and its accumulation in the blood (13). Healthy individuals have a half-life of 15-30 minutes and serum level of Lactate 2-0.8 mmol/L (14). Monitoring serum lactate levels as a marker of metabolic disorders is very important due to the advantages of high sensitivity, real information about tissue secretion, oxygen demand and convenient disposal to outcomes (12).

Blood lactate accumulation in different age groups of hospitalized traumatic patients is an indicator item for pre-hospital conditions and independent marker in predicting the severity of injury and mortality (15). If lactate predicts morbidity and mortality in traumatic patients, it can be used to improve the triage protocol during hospital admission (16). So far, several studies have been published on the positive association between lactate and mortality in adults with trauma, but there is not enough research in multi traumatic children. On the other hand, time is a valuable element in the management of traumatic children, and it is becoming increasingly important to have an index that is easier to measure, cheaper and more accessible.

The aim of this study was to investigate the association between serum lactate level and mortality rate in multi-traumatic children in the emergency department of Shuhada and Imam Reza hospitals, affiliated with Tabriz University of Medical Sciences, Northwestern Iran.

2- MATERIALS AND METHODS

2-1. Study design and population

This cross-sectional analytical study has been performed on all multi-traumatic children who were referred to the emergency department of Shuhada and Imam Reza hospitals in Tabriz University of Medical Sciences (as training and referral hospitals) from March 2018 to March 2020. This study was performed on Azeri Turks, who are members of one of the largest ethnic groups in Iran (17, 18).

All children with multi-trauma were evaluated using the census method. The variables were included age, sex, diagnosis

at hospitalization, the severity of trauma at hospitalization, outcome (dead, alive), serum lactate, and other tests related to chemical profiles as well as the condition of consciousness. The data gained by interview, the examination of children and the result of tests.

2-2. Laboratory measurements

The evaluation of short-term and final status of patients was performed based on serum lactate level and discharge status (death and recovery) respectively.

At the time of admission, the intravenous blood sample was immediately provided to determine lactate level by an auto-analyzer system that was calibrated daily. The normal range for lactate is between 0.5 and 2.5 mmol/L.

The trauma severity was determined based on the PRISM table (19). The PRISM score was calculated based on age, systolic blood pressure, heart rate, body temperature, papillary eye reflexes, mental and consciousness state, arterial blood test and laboratory examination results (**Appendix 1**). The classification was based on scores (0-5, 6-10, 11-15, 16-20, 21-25, 26-30, 31-35, and >35) with the range of 0 to 74. The elevated PRISM score was correlated with a higher mortality rate.

2-3. Procedure

In the first 2 hours of admission, demographic information and 10 cc of intravenous and intra-arterial blood (for the determination of lactate, and other laboratory tests) and intrastate was obtained from eligible children for laboratory tests. The illness severity was determined based on the PRISM score. Then, children grouped according to outcome (dead and alive) and lactate levels (0-2, 2-4, 4-6, 6-8, 8-10, and >10) and associations between the results and groups were investigated.

2-4. Inclusion and exclusion criteria

The inclusion criteria were as follows: 1) desire to participate in the study, 2) age < 14 years (with the agreement of specialists), 3) Children injured as a consequence of road traffic accidents or falls, 4) children with multi-trauma, i.e. those suffering from many injuries and accidents (2). 5) Children in need of air way care and protection or peripheral circulation. Exclusion criteria were the followings: 1) the lake of cooperation, 2) patients with a history of malignancy or underlying infection, 3) injuries as a result of other causes such as drowning, burns, poisoning, or animal bites, 4) dying during the study, 5) age>14 years old

2-5. Data Analyses

For descriptive statistics, mean and standard deviation were used to describe quantitative variables; and frequency and percentage were used for qualitative variables.

For analytical statistics, Chi-square test, independent samples t-test, ANOVA test, and Simple and multivariate logistic regression tests were performed in SPSS.22. P-value<0.05 and OR with 95% confidence interval were considered statistically significant.

3- RESULTS

3-1. Patients

At first, 135 children were included in the study. Twenty-five children were excluded due to various reasons, including patients' dissatisfaction to participate in the study, discharge from the hospital with personal consent, and failing to provide a blood sample during the mentioned period. The demographic characteristics are shown in **Table 1**.

The most common cause of hospitalization was road accidents along with falling from heights; and the frequent injuries were thorax damage and fractures. Serum lactate

level was measured in all patients admitted to the hospital emergency department in the first 2 hours. The mean lactate level was 3.2 mmol/L with a range between 0.6 to 28.3 mmol/L when 85 (77.2%) patients had blood lactate level> 2 mmol/L (Table 1&3).

Table-1: Demographic characteristics of multi-traumatic children

Variables		Value
Sex	Male	57(51.8%)
	Female	53 (48.1%)
Age	Mean ± SD	7.7 ± 4.2
Outcome	Dead	10 (9%)
	Alive	100 (91%)
Need for intubation	Frequency (%)	96 (87.2%)
Serum lactate level (mmol/L)	Mean	3.2 mmol /L
	Min-Max	0.6 to 28.3 mmol/L

SD: Standard deviation, Min: Minimum, Max: Maximum, (%): percentage

3-2. The association of the outcome (dead and alive children with multitrauma) with lactate level and other factors

There was a significant difference between groups (dead and alive children) in terms of lactate concentration. As shown in **Table 1**, the mortality rate was significantly associated with high concentrations of serum lactate. Other factors and their association with mortality are listed in **Table 2**.

Table-2: The association of the outcome (dead and alive children with multitrauma) with lactate level and other findings

Variables	Dead children N=10	Alive children N=100	P-value
Age (Year)	5.3	6.8	0.68
PRISM score (mean)	28	18	<0.001
Need for intubation F(%)	10 (10%)	86 (86%)	<0.001
Lactate (mmol/l)	6.6	3.1	<0.001
Albumin (g/l)	36.5	42.6	<0.001
Blood sugar (mg/dl)	10.1	7.12	<0.001
Creatinine (mg/dl)	1.7	0.9	<0.001
Bilirubin (mg/dl)	8.3	6.8	<0.001
Bicarbonate (meq/L)	17.3	20.8	<0.001
PH	7.35	7.41	<0.001

PRISM: Pediatric Risk of Mortality. F (%): Frequency (percentage)
Analytical statistics: Chi-square test, and independent samples t-test

3-3. The association of blood lactate levels with demographic findings and laboratory tests

There was a significant difference among groups (0-2, 2-4, 4-6, 6-8, 8-10, and >10 lactate levels) in terms of demographic findings and laboratory tests.

Higher mortality rate, PRISM scores, blood sugar, and low bicarbonate level and blood pH were significantly associated with elevated lactate levels (**Table 3**).

Table-3: The association of blood lactate levels with demographic findings and laboratory tests (six groups)

Variables	G1	G2	G3	G4	G5	G6	P-value
Lactate (mmol/L)	0-2	2-4	4-6	6-8	8-10	>10	
Frequency	25	47	21	8	4	5	P<0.001
Age (year)	5.3	6.5	5.8	5.9	4.6	4.1	P<0.001
PRISM (mean)	11	13	16	19	27	31	P<0.001
Need for intubation (Frequency)	16	45	18	8	4	5	P<0.001
Blood sugar (mg/dl)	6.5	6.9	7.3	8.8	12.3	15.8	P<0.001
Bicarbonate (meq/L)	21.4	19.7	17.4	15.6	13.7	11.2	P<0.001
PH	7.43	7.32	7.31	7.24	7.21	7.05	P<0.001

G: group
Analytical statistics: ANOVA test

3-4. Results of univariate and multivariate regression models

The analysis of univariate and multivariate regression models showed that an increasing serum lactate could be independently associated with increased hospital mortality.

Univariate regression analysis that was calculated based on sample size, gender, blood lactate, creatinine, albumin, PH and blood sugar levels showed that for each one mmol/l increase in blood lactate level, the odds for in-hospital mortality increased by 38% (OR = 1.38; 95% CI, 1.30-1.46; p <0.001). This association was observed even after matching the variables, as the mortality rate increased with increasing lactate level (OR = 1.27; 95% CI, 1.19-1.35; P <0.001). (Table 4)

Multiple regression model showed that increase in serum lactate level (OR = 1.17; 95% CI, 1.07-1.29; p = 0.001), increase in PRISM score (OR per 1-point increase = 1.15; 95% CI, 1.11-1.20; p <0.001) and decrease in serum albumin (OR per 1 g / l increase = 0.92; 95% CI, 0.98- 0.88- p <0.001) are independent risk factors in the mortality rate of traumatic children. (**Table 4**). Blood lactate level with a sensitivity of 61% and a specificity of 86% is an important predictor in assessing the mortality rate of patients with a cut-off of 5.55 mmol/l.

Table-4: Comparison of univariate and multivariate regression models in multi traumatic children

Variables	Univariate regression analysis		Multivariate regression analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age (year)	1.58 (1.07-2.33)	0.021	1.11 (0.63-1.97)	0.715
PRISM (mean)	1.18 (1.15-1.21)	<0.001	1.15 (1.11-1.20)	<0.001
Lactate (mmol/l)	1.38 (1.30-1.46)	<0.001	1.17 (1.07-1.29)	<0.001
Albumin (g/l)	0.86 (0.83-0.89)	<0.001	0.92 (0.88-0.96)	<0.001
Creatinine (mg/dl)	1.01 (1.00-1.01)	<0.001	0.99 (0.98-1.01)	<0.488
Bilirubin(mg/dl)	1.01 (1.00-1.01)	<0.001	0.92 (0.88-0.96)	<0.665
Bicarbonate (meq/L)	0.89 (0.87-0.93)	<0.001	1.03 (0.98-1.08)	<0.567
PH	0.01 (0.00-0.03)	<0.001	0.54 (0.06-4.75)	<0.445

OR: odds ratio,
Analytical statistics: Regression analysis.

4- DISCUSSION

In the present study, blood lactate level in multi traumatic children was evaluated on the first two hours of admission at the emergency department. The results showed that the mortality rate increased with elevated blood lactate level which can be considered as a predictor variable in multi traumatic children. Several studies have shown that higher concentrations of blood lactate as a predictor index in traumatic adults are associated with an increasing in-hospital mortality. Lactate concentration more than 5 mmol/L and pH > 7.25 generally indicate Hyperlactatemia (19, 20).

In a study conducted by Bernhard et al., 532 traumatic patients admitted to the hospital emergency department found that more than 2 mmol/l increase in lactate level has been accompanied with a mortality of 22.7% and the mortality rate was more noticeable with more than 8 mmol/l increase in lactate level. Therefore, the high levels of lactate at admission are associated with an increase in mortality in 24 hours and 30 days, and lactate can be used to predict mortality rates and identify critically ill patients (21).

In another study, Safari et al. found that elevated serum lactate levels, heart rate and PCO2 were significantly associated with a high mortality rate in 250 multi traumatic patients with 14.8% hospital mortality; so these factors were considered as early predictors related to in-hospital mortality (22). On the other hand, in the study by Koliski et al. (23) and Salvo et al. (24), other factors were preferred instead of the lactate element as important factors for assessing and predicting mortality. In our point of view this difference may be due to having a small sample size, not evaluating other variables simultaneously on a large scale, or checking factors the measurement of which should be conducted over a long period of time and requires more advanced techniques; thus, lactate still remains the initial evaluation factor for traumatic patients.

In the present study, besides lactate, other factors were examined, including the PRISM element. An accurate clinical prognostic tool for pediatric mortality could be considered PRISM and lactate level due to high sensitivity tests and evaluation on the first day (25).

Blood sugar was another factor examined when hyperglycemia was observed with hyperlactatemia (elevated serum lactate). In diabetic patients with septicemia, it is reported that hyperlactatemia and hyperglycemia (26) have been seen commonly in severe traumatic patients. However, in the assessment of mortality, hyperglycemia cannot be considered as an independent prognostic factor similar to hyperlactatemia. It can be valuable along with hyperlactatemia. In addition, multivariate analytical studies have shown that the arterial PH is valuable for management; however, it could not independently act like hyperlactatemia (27).

This study was designed to determine the association between hyperlactatemia and mortality in traumatic children. Previous studies have suggested that traumatic children should be more closely monitored with lactate levels above 2.5 mmol/L (28). In our study, about 65% of patients had lactate levels above 6.5 mmol/L, which was important for mortality prediction (29). In our study, serum glucose and bicarbonate were respectively higher and lower, in deceased individuals than in living individuals; however, they were not considered as risk factors in the regression model. In a study conducted by Yue-qiang Fu et al, on two hundred and thirteen traumatic children, admission lactate was independently associated with mortality rate, but admission glucose was not an independent risk factor for death. However, admission lactate and glucose were significantly higher in non-survivors

than in survivors (30). In another study, Salas Ballestin et al, investigated the prognostic factors in 131 patients hospitalized in the pediatric intensive care unit (PICU) after drowning. Patients who required advanced resuscitation with epinephrine were lower bicarbonate, PH, temperature, and Glasgow Coma Scale score, and higher glucose levels during admission (31). Therefore, it is suggested to conduct further studies with larger sample sizes for other factors such as bicarbonate and glucose in addition to lactate.

5- STUDY LIMITATIONS

The limitations of this study were as follows: 1) Blood lactate assessment was not performed continuously and serially, 2) Patients could be studied in wider specialized fields.

6- CONCLUSIONS

In this study, we concluded that initial hyperprolactinemia may have an independent association with in-hospital mortality rate, even at different levels in multi-traumatic children. Other items, such as PRISM score, blood sugar (BS), bicarbonate, and PH are associated with mortality rate in these children. Therefore, in order to select an effective service delivery for multi-traumatic patients with hyperprolactinemia or elevated PRISM score, it is essential to check BS at the first admission in the emergency room.

7- ETHICAL CONSIDERATIONS

This study was performed after receiving the ethical code of the Vice Chancellor for Research Ethics Committee of Tabriz University of Medical Sciences. The instructions of the Helsinki Declaration were observed during the study. Permission from participants or parents was obtained for receiving the blood sample, completing the questionnaire and following up the short-term mortality. No additional cost was taken from the patients. Patients' information and their identities were kept confidential.
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8- COMPETING INTERESTS

None.

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