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# Investigation of Frequency of the Lethal Triad and Its 24 Hours Prognostic Value among Patients with Multiple Traumas

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**Abstract**

**BACKGROUND:** Death in multiple trauma (MT) patients is one of the serious concerns of the medical service provider. Any prediction of the likelihood of death on the assessment of the patient's condition is performed using different variables, one of the tools in the triage of patients to determine their condition.

**AIM:** We aimed to investigate the frequency and the predictive value of death in 24 hours triad of death in patients qualified with multiple traumas admitted to Imam Khomeini hospital.

**METHODS:** This was a prospective cross-sectional study to determine the prevalence and predictive value of 24-hour triad of death among patients with MT referred to an emergency department. Three factors including acidosis, hypothermia and coagulopathy and predictive value of 24-hour death were evaluated. Arterial blood gas, oral temperature and blood samples for coagulation factors were analysed. Data were analysed using SPSS version 19. Multivariate analysis (logistic regression) was used to determine the predictive value of the triad of death.

**RESULTS:** A group of 199 MT patients referring to Imam Khomeini hospital during the first 6 months of 2015 were evaluated for the first 24 hours of admission. Logistic regression analysis showed that using the following formula based on the triad of death can predict death in 96% of cases can be based on the triad of a death foretold death upon admission to the emergency room. It should be noted that this prediction tool as 173 people left alive after 24 hours as live predicts (100% correct).

**CONCLUSION:** The triad of death is one of the tools in the triage of patients to determine their condition and care plan to be used, provided valuable information to predict the prognosis of patients with a medical team.

## Introduction

Death in multiple trauma patients referring to hospitals is one of the serious concerns of the medical service providers. For this reason, any prediction of the likelihood of death on an assessment of the patient's conditions performed using different variables, one of the tools in the triage of patients to determine their condition and care planning is used and as well as valuable information to predict the prognosis of the treatment team [1].

Trauma deaths divide into three categories: immediately at the scene, within the first 24 hours during initial resuscitation, and in the next 3 to 4 weeks as a result of multiple organs failure. Failure to resuscitate adequately in the emergency department can lead to acidosis, hypothermia, and coagulopathy, which can result in multiple organs failure and cause death in these patients [2], [3].

Major trauma patients may develop a tendency to bleeding diathesis, which results in defective clotting and platelet function. If patients require > 10 units of packed red blood cells (PRBC), patients should receive PRBC in a 1:1 ratio with fresh frozen plasma (FFP). Both acidosis and hypothermia contribute to the coagulopathy and should be corrected as soon as possible [4], [5].

The fundamental problem in patients, who need damage control procedures, is the shock due to trauma. This is due to hypovolemia caused by bleeding and tissue damage caused by a large amount of energy transmitted through the affected organism. The shock caused by trauma leading to hypoperfusion and inflammatory cascade is activated. Metabolic acidosis and hypothermia result in worse induced coagulopathy or loss of coagulation factors. Although the triad of hypothermia, acidosis and coagulopathy may be fatal in certain circumstances, one or more of this death may play a protective role. A lot of press (publications) has supported the notion that significant hypothermia may protect the organism from severe hypoperfusion. Oxygen dissociation curve is shifted to the right with acidosis. This allows better oxygen removal in the tissue [6]. The clotting cascade is comprised of serine proteases whose activity is pH dependent. It has been widely established that acidosis is a common consequence of acute injury (locally and systemically). It is also known that severe acidosis impairs the efficiency of the clotting cascade. Thromboelastography (TEG) is a sensitive means of assessing the interaction of all parts of the clotting cascade as they work in concert. In a large trial of general surgery patients undergoing large volume blood loss surgery (500 cc), the presence of hyperchloremic acidosis correlated with the development of coagulopathy. Exvivo data evaluating the impact of high chloride solutions on the TEG profile also indicates clotting dysfunction when the serine proteases are in a Cl2 rich and academic environment [7].

Coagulability is destroyed with hypothermia. So despite normal PT and PTT, clinical coagulability may exist. Often coagulability relief when the patient is again rewarmed, although some cases of DIC rarely reported. Multi factors play a role in impairing the coagulability; consisting of blood concentration, vessel constriction and releasing of tissue thromboplastin from cold ischemic tissue. Deposited fibrinogen due to hypothermia may increase the risk of cardiac and cerebral thrombosis. Hypothermia induces bone marrow suppression and splenohepatic sequestration. This decreases platelet and leukocyte. Leucopenia and thrombocytopenia relieve when the patient is again rewarmed [8].

We aimed to investigate the frequency and the predictive value of death in 24 hours triad of death in patients qualified with multiple traumas admitted to Imam Khomeini hospital.

## Methods

### *Study design*

The present cross-sectional and prospective was carried out on the triad of death to determine the prevalence and predictive value for 24 hours in multiple trauma patients admitted to ED of Imam Khomeini Hospital, Sari, Mazandaran, Iran. The duration of the study was in the first 6 months of 2015. Protocol of this study was approved by the ethics committee of Mazandaran University of Medical Sciences after evaluation in the research council of emergency medicine specialists group. Registration thesis number is 870 at Mazandaran University of Medical Science. To maintain the confidentiality of patients' medical profile data and to adhere to ethical practice, the researchers keenly adhered to the principles introduced in the declaration of Helsinki during the study period. Information regarding the study method was given to the participants, and written consent was obtained from them before being included in the study.

### *Participants*

The subjects in the present study consisted of patients with Multiple Trauma were enrolled due to the inclusion and exclusion criteria, who had referred to the emergency department (ED). The patients' GCSs was recorded on admission time and the mean systolic blood pressure of patients at presentation measured. In this study, the median heart rate of patients on admission accounted for the average number of respiratory rate, the median oxygen saturation ($O_2$sat). Among the vital signs upon arrival, only the respiratory rate had a significant correlation with the mortality rate.

### *Data collection*

A senior emergency medicine resident was responsible for gathering data of the patients by completing a pre-designed checklist including baseline characteristics (Age, sex**,** GCS**,** systolic blood pressure, Heart Rate, Number of respiratory rates, $O_2$sat).

Considering that approximately 400 multiple trauma patients in Imam Khomeini hospital in Sari employ and with the prevalence of 25 to 35 per cent of the triad of death, And by taking a 30% prevalence rate for the calculation of sample size and accuracy of 4.5%, The number of samples required to determine the prevalence of the triad of death will be about 200 people. The three factors triad of the death of the patients was being evaluated at the beginning and six hours later. The first factor, acidosis, in the PH range of less than 7.36 and less than 7.15 were being assessed. The second factor is coagulopathy for which PT; PTT & PLT were be used. The third factor is hypothermia. Follow-up of these patients will be done by the investigator (Emergency Medicine Resident), and a questionnaire was be completed by him.

### *Statistical Analysis*

The sample size was determined based on presenting with multiple trauma patients. After data collection, the data were statistically analysed using SPSS 21 statistical software. The data describe the mean and standard deviation for quantitative variables and the number and percentage for qualitative variables were being used. To determine the predictive value of the triad of death, multivariate analysis (logistic regression) was to being used. The significance level was 0.05.

## Results

In this study, 199 multiple trauma patients referring to Imam Khomeini hospital emergency department during the first 6 months of 1394 were evaluated for the first 24 hours of admission. Patients included 155 males (77.9%) and 44 women (22.1 per cent). The average age for men was 35.5 years (SD Rules 15 years), with a minimum of 18 and a maximum of 60 years.

The average female patient age was 35.6 years (SD Rules 13.8 years), with a minimum of 13 and a maximum of 60 years. Among male patients, 21 patients (13.5%) and among female patients, 5 patients (11.4%) died (Table 1).

**Table 1: Gender and Death 24h Cross tabulation**

| | | | Death 24h | | Total |
|---|---|---|---|---|---|
| | | | Alive | Death | |
| Gender | Female | Count | 39 | 5 | 44 |
| | | % within Gender | 88.6% | 11.4% | 100.0% |
| | Male | Count | 134 | 21 | 155 |
| | | % within Gender | 86.5% | 13.5% | 100.0% |
| Total | | Count | 173 | 26 | 199 |
| | | % within Gender | 86.9% | 13.1% | 100.0% |
| | | % within Death24h | 100.0% | 100.0% | 100.0% |

Using this formula, 19 cases predicted as mortality (73.1%) and 7 cases predicted as alive (26.9%). It should be noted that this prediction tool as 173 people left alive after 24 hours as live predicts (100% correct) (Table 2)**.**

**Table 2: Death 24h Statistics**

| Death 24h | | Age | SBP | GCS | PT | PTT | PLT | pH | T | WBC | Hb |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Alive | N Valid | 173 | 173 | 173 | 173 | 173 | 173 | 173 | 173 | 173 | 173 |
| | Mean | 35.02 | 117.77 | 14.32 | 12.14 | 30.06 | 238438.15 | 7.35 | 36.676 | 11097.69 | 12.72 |
| | Median | 30.00 | 120.00 | 15.00 | 12.00 | 30.00 | 242000.00 | 7.34 | 37.000 | 10500.00 | 12.90 |
| | Std. Deviation | 13.640 | 18.051 | 2.259 | .419 | 2.666 | 75339.820 | .048 | .4940 | 4143.164 | 1.764 |
| Death | N Valid | 26 | 26 | 26 | 26 | 26 | 26 | 26 | 26 | 26 | 26 |
| | Mean | 39.46 | 79.81 | 5.23 | 26.93 | 75.77 | 109307.69 | 7.19 | 35.081 | 20215.38 | 8.53 |
| | Median | 37.50 | 67.50 | 5.00 | 27.00 | 64.00 | 90000.00 | 7.18 | 35.000 | 18350.00 | 8.50 |
| | Std. Deviation | 16.090 | 27.477 | 2.612 | 10.168 | 29.144 | 46063.234 | .103 | .1167 | 7359.440 | .925 |
| | P-VALUE | 0.198 | < 0.0001 | < 0.0001 | < *0.0001* | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 |

SBP = Standard Blood Presure; GCS = Glasgow Coma Scale; PT = Prothrombin Time; PTT = Partial Thromboplastin Time; PLT = Pelatelet; T = Temperature; WBC = White Blood Cell; Hb = Hemoglobin.

In this study, 26 patients (13.1%) died; of which all (100%) hypothermic 173 people were survived out of which 2 cases (1.2%) were hypothermic. The Difference was statistically significant (p-value <0.0001) (Table 3).

**Table 3: Hypothermia Statistics**

| Hypo-thermia | | Age | SBP | GCS | PT | PTT | PLT | pH | T | WBC | Hb |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No Hypo-thermia | Valid | 171 | 171 | 171 | 171 | 171 | 171 | 171 | 171 | 171 | 171 |
| | Missing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Mean | 35.09 | 117.83 | 14.43 | 12.13 | 30.04 | 238952 | 7.35 | 36.693 | 11112 | 12.76 |
| | Median | 30.00 | 120.00 | 15.00 | 12.00 | 30.00 | 242000 | 7.34 | 37.000 | 10500 | 12.90 |
| | Std. Deviation | 13.694 | 17.901 | 2.020 | .396 | 2.665 | 749025 | 0.048 | 0.4696 | 4156 | 1.744 |
| Hypo-thermia | Valid | 28 | 28 | 28 | 28 | 28 | 28 | 28 | 28 | 28 | 28 |
| | Missing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Mean | 38.75 | 82.14 | 5.21 | 25.93 | 72.64 | 115392 | 7.20 | 35.089 | 19475 | 8.63 |
| | Median | 36.00 | 72.50 | 5.00 | 24.00 | 64.00 | 90000 | 7.19 | 35.000 | 15500 | 8.50 |
| | Std. Deviation | 15.773 | 28.785 | 2.573 | 10.448 | 30.307 | 56157 | 0.108 | 0.1286 | 7617 | 0.990 |
| | p-value | 0.278 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |

SBP = Standard Blood Presure; GCS = Glasgow Coma Scale; PT = Prothrombin Time; PTT = Partial Thromboplastin Time; PLT = Pelatelet; T = Temperature; WBC = White Blood Cell; Hb = Hemoglobin.

In this study, 26 patients (13.1%) died. Among them, 25 patients (96.2%) had PH <7.36.173 patients (86.9%) survived, of which 114 (65.9%) had PH <7.36, respectively**.** The difference was statistically significant (p-value = 0.002) (Table 4).

**Table 4: Acidosis and Death 24h Cross tabulation**

| | | | Death 24h | | |
|---|---|---|---|---|---|
| | | | Alive | Death | Total |
| Acidosis | >7.36 | Count | 59 | 1 | 60 |
| | | % within Acidosis | 98.3% | 1.7% | 100.0% |
| | | % within Death24h | 34.1% | 3.8% | 30.2% |
| | <7.36 | Count | 114 | 25 | 139 |
| | | % within Acidosis | 82.0% | 18.0% | 100.0% |
| | | % within Death24h | 65.9% | 96.2% | 69.8% |
| Total | | Count | 173 | 26 | 199 |
| | | % within Acidosis | 86.9% | 13.1% | 100.0% |
| | | % within Death24h | 100.0% | 100.0% | 100.0% |

Using this formula, 19 cases predicted as mortality (73.1%) and 7 cases predicted as alive (26.9%). It should be noted that this prediction tool as 173 people left alive after 24 hours as live predicts (100% correct).

## Discussion

In this study, the frequency and the predictive value of death in 24 hours triad of death were investigated in patients qualified with multiple trauma admitted to Imam Khomeini hospital. This centre has so far studied to determine the frequency of the triad of death which has not been done in patients with multiple trauma. Due to this fact that in sari's Imam Khomeini hospital, there is no registry trauma unit and to provide more accurate services to multiple trauma patient, it is helpful to determine the severity of injury, in this study, we investigated patients with Multiple trauma for the presence of three factors of acidosis, hypothermia and coagulopathy and aimed to find the relationship between these factors and fatality rate among Patients with Multiple Trauma [9], [10]. Trauma deaths divide to three categories: immediately at the scene, within the first 24 hours during initial resuscitation, and in the next 3 to 4 weeks as a result of multiple organs failure [11], [12]. Failure to

resuscitate adequately in the emergency department can lead to acidosis, hypothermia, and coagulopathy, which can result in multiple organs failure and cause death in these patients [6], [13]. Most hospitals obtain a standard panel of labs in every trauma patient, although in many cases, these have little impact on the initial management [14], [15]. Critical labs in patients with major trauma include a baseline hematocrit, platelet count, blood clot for typing, pregnancy test, and coagulation panel. Laboratory evaluation of the trauma patient can provide an objective measure of the adequacy of resuscitation. It also provides much-needed information for proper transfusion products and the onset of coagulopathy.

The fundamental problem in patients, who need damage control procedures, is the shock due to trauma. This is due to hypovolemia as a result of bleeding and tissue damage caused by a large amount of energy transmitted through the affected organism. The shock caused by trauma leading to hypoperfusion and inflammatory cascade is activated. Metabolic acidosis and hypothermia result in worse induced coagulopathy or loss of coagulation factors. Although the triad of hypothermia, acidosis and coagulopathy may be fatal in certain circumstances, one or more of these deaths may play a protective role 15. We have in contrast to previous studies, patients were 13-60 years.73.1% of the victims had platelet disorders, 100 per cent had abnormal PTT, and 92.3% had abnormal PT. This is in line with the results of previous studies 16 and unfortunately of 199 patients with multiple trauma triad of death, 26 people died within the first 24 hours from the moment of admission, also the primary systolic blood pressure mean was significantly low in victims [17], [18]. Similar results are found in study investigation the significant relation between anaemia and mortality and all of the patients with multiple traumas were anaemic because this study determined that Trauma is a serious global health problem, accounting for approximately one in 10 deaths worldwide. Uncontrollable bleeding accounts for 39% of trauma-related deaths and is the leading cause of potentially preventable death in patients with major trauma. While bleeding from vascular injury can usually be repaired surgically, coagulopathy-related bleeding is often more difficult to manage and may also mask the site of vascular injury. The causes of coagulopathy in patients with severe trauma are multifactorial, including consumption and dilution of platelets and coagulation factors, as well as dysfunction of platelets and the coagulation system. The interplay between hypothermia, acidosis and progressive coagulopathy, referred to as the 'lethal triad', often results in exsanguinations [19].

Similar results are found in study investigation the low primary systolic blood pressure, low GCS score and coagulopathy were associated with increased mortality [20], [21], [22].

We have in contrast to previous studies the mortality rate was 100% in patients with impaired PTT and patients who were impaired in PT and patients with platelet disorders were 77.4% and 79.2%, respectively and there was no significant correlation between age and mortality. The mean GCS for women was 13.98 (SD = 2.88). The mean GCS in men was 12.9 (SD = 4.04). The difference was statistically significant (p-value = 0.048) [23], [24], [25].

Finally, this research showed us the necessity of having a trauma registry in Sari's Imam Khomeini hospital which can be a great help in evaluating of patients with multiple trauma who have the factors with high predictive value for the 24-hour death. Identification of abnormal levels of these factors in the time and effort to correct it within 24 hours of acceptance had a major role in preventing the premature death of the patients. Some limitations was in this study.

In conclusion, this research could be the basis for further studies to examine the effects of these factors on the rate of mortality in patients with Multiple Trauma.

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## Author' s Contribution

All authors passed four criteria for authorship contribution based on recommendations of the International Committee of Medical Journal Editors.

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