



# **An Analytical Study on Acute Liver Injury in Patients Caused by Classic Heat stroke**

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## **Authors' contributions**

*This work was carried out in collaboration between both authors. All authors read and approved the final manuscript.*

## **Article Information**

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## **ABSTRACT**

Heat Stroke is a kind of medical emergency that can cause severe dehydration and neurological changes as a result multi-organ injuries or failure could be possible. Heat strokes occur when the body temperature exceeds 40 °C due to external heat and humidity. The liver is widely affected by heatstroke that's why taking care of patients suffering from heatstroke is very important. Various studies have been reported in the literature regarding acute liver failure but none of the studies discussed acute liver failure during the hospital stay. Patients during their hospital stay will have a higher risk of mortality due to heatstroke. In this paper, an analytical study has been done on admitted patients to a government hospital in India. These patients are suffered from heatstroke from April 2007 to September 2011 and a second time period from July 2018 to September 2019. The sample includes 60 patients with 58 (97%) males having a totaled number of 12 fatalities. The observed International Normalized ratio (INR) parameter is greater than 1.6 and no increased mortality has been noticed, aspartate aminotransferase (AST), as well as alanine aminotransferase (ALT) levels, were not associated with an increased mortality rate.

**Keywords:** *Acute liver failure; core body temperature; heat stroke; intravascular cooling; mortality.*

## 1. INTRODUCTION

Heat stroke is defined in terms of core body temperature greater than 40°C caused hot, dry skin and central nervous system abnormalities including coma, delirium and convulsions. Heat stroke is a severe medical condition and common at warm places [1]. There are mainly two types of the heat stroke: (i) Classic heat stroke and (ii) heat stroke induced by exercise. The classic heat stroke mainly caused by exposure of body at high temperature without involving any physical exercise or activity [2]. On the hand, exercise induced heat stroke occurs due to the physical activity. Athletes are widely suffered from exercise induced heat stroke. Heat stroke can cause injury and damage to many body organs including muscles, kidney, liver, heart and lungs. Classic heat stroke is very dangerous as compared to heat stroke caused by the exercise because it doesn't require any physical activity; it's just depending on the environmental condition [3]. At warm places, main cause of death of many peoples is due to the heat waves caused by classic heat stroke. Most of the people die in their homes and some of those who are admitted to the hospital needs intensive care and their mortality can increase above 60% and in rare case some patients suffer from permanent neurologic damage [4]. Various changes have been observed in the body under the heat stroke condition that can be understood by pathogenesis and pathophysiology.

Acute liver injury (ALI) is one of the most common problem associated with the classic heat stroke. When the temperature of the body suddenly changes, the cells of the body react quickly and start producing heat stress or heat shock proteins. Under the heat stress, more than one heat shock transcription factors bind to the heat-shock components as a result rate of producing of heat-shock proteins [5]. The increment of the heat shock proteins in the cell can cause the damaging of tissues and antibodies as well as liver cells. Due to the classic heat stroke, it could damage the structure and functions of the many essential molecules of the body include nucleic acids, lipids and proteins, as a result cells and tissues of the body are badly affected that can cause severe medical emergency condition. Acute liver injury/failure is one of the medical condition that is severely affected by the classic heat stroke [6]. Acute liver failure (ALF) or injury is due to the presence of coagulopathy (INR $\geq$  1.5) that caused by any degree of hepatic encephalopathy, medically

defined by the West Haven criteria. The liver cell injured due to the coagulopathy development (caused by classic heat stroke) that consist fibrinolytic and anticoagulant system imbalance, reduction in synthesis of procoagulant factors and platelet dysfunction. Acute liver disease compromises brain metabolism by raising cerebral flow, oxygen metabolism reduction and impairing mechanism of self-regulation of the cerebrovascular [7]. It produces Neuroinflammation that stimulates the microglia to produce interleukin and tumor necrosis factor-alpha (TNF-alpha) Encephalopathy of the liver.

The present study discussed about the effect of classic heat stroke on liver that can cause acute liver failure/injury to hospitalized patients. The study has been done on admitted patients (suffered from classic heat stroke) during their stay to a government hospital in India. This study mainly focused on the evaluation of patients who developed acute liver injury/failure during hospital stay and maintain high mortality rate.

## 2. LITERATURE REVIEW

Various studies have been done in the literature in order to establish the relationship between acute liver disease and heat stroke. Most of the studies done for the exercise induced heat stroke and very less literature are available for acuter liver failure/injury caused by classic heat stroke. *Prof. Jin* and his team reported that exertional heat stroke leads to acute hepatic failure that is very uncommon symptoms in the patients. At the time of liver transplant, acute hepatic failure is still need to address that caused by exertional heat stroke [8]. In another research, a case study has been done for the acute kidney injury caused by heat stroke on a 14-year-old healthy patient. When the patient was exercising, high fever and acute seizures has been observed. These symptoms can result into body organs failure [9].

*Prof. Roger* have done neuropathologic investigations for acute liver failure (ALF) that shows changes in neuroglia that consist of astrocytes swelling that caused edema of cytotoxic brain and intracranial hypertension. When the ammonia concentration increase in arterial of patients with acute liver failure is the indication of risk of the brain herniation [10]. Hepatic encephalopathy and coagulopathy are responsible for the acute liver failure. In order to functionalize the liver in hemostasis, coagulopathy is an important component that reflects the central role. For the Acute liver failure

diagnosis, INR  $\geq 1.5$  was required. Moderate coagulopathy in Acute liver failure caused is about little concern but in the case of severe coagulopathy, the bleeding can be major hurdle in order to treat patients with Acute liver failure [11].

In another research, scientist was mentioned that heat stroke is a rare problem, but it can cause severe medical emergency in the peoples during summers. The patients who suffered from acute liver failure or acute liver injury had rhabdomyolysis and lactic acids. In order to cure the patients, there are various treatments given to patients such as cooling treatment, mechanical ventilation and N-acetyl cysteine (NAC), renal replacement and liver transplant surgery. Some patients were died also [12]. The people who live at warm places, most of the people suffer from the increased level of serum in liver enzymes. It is recommended as liver transplant is necessary in the case of severe liver failure. After the transplant surgery, it is difficult for the people to survive in long-term in exertional heat stroke. In the case study, a man got heat stroke after running 5 km at 21 °C as a result serum alanine aminotransferase (ALAT) activities increasing to 16,410 U/l after two days that causes severe liver damage. The patient referred for liver transplant surgery but cured completely with conservative treatment [13]. The reported studies in the literature only discussed about the impact of heat stroke on liver functionality based on the variation in biochemical in the normal conditions but none of the studies discussed about the impact of heat stroke in liver injury during the hospital stay. The patients who admitted to the hospital have higher risk of mortality due to heat stroke. Due to this reason, this case study has been done in order to evaluate the mortality rate caused by acute liver injury due to heat stroke while patients staying in the hospital.

### 3. METHODOLOGY

#### 3.1 Research Design

The analytical study of admitted patients to a government hospital in India has been conducted who had classic heat stroke in different time periods i.e. from April 2007 to September 2011 and a second time period from July 2018 to September 2019. There has been 7 years gap in between the first and second cohort, this is because many patients' files has been lost and electronic files starts maintaining from 2016. In

this study, the patients (diagnosed with heat stroke) were included who admitted to the hospital's emergency department. In this study, central body temperature  $\geq 40$  °C referred as heat stroke that caused by exposure to high environmental temperature.

For this study, the patients were selected on the basis of specific criteria related to the age, sex and date of admission as well as laboratory studies including blood cytometry and chemistry, liver function panel, coagulation tests. The selected patients were male and age lies between 25-45 years. The patients suffered from diseases related to heart, kidney and lungs were excluded from this study.

#### 3.2 Sample and Instrument

In this case study, the sample includes 60 patients with 58 (97%) male having totaled number of 12 fatalities. The quantitative analytical study has been performed based on International Normalized ratio (INR) parameter in order to evaluate the mortality rate.

#### 3.3 Data collection and Analysis

The data was collected on the basis of medical records that has been collected and preserved by the fellow medical resident during those years in hospital. The patients for this study was only selected on the basis of age, sex, date of admission, coagulation tests, blood cytometry and chemistry, liver functional panel and mortality.

In order to analyze the data, standard deviation (SD) and mean or interval and median used to express the quantitative variables. For the comparison the continuous variables, scholar's t-test was used. Spearman's correlation coefficient test was used for the analysis of quantitative variables. The categorical variables were represented in terms of percentages and frequencies.  $\chi^2$  test done in order to compare proportions.  $p < 0.06$  was considered as statistically significant value.

### 4. RESULTS AND DISCUSSION

A sample of 58 (97%) male patients has been taken for the case study. Due to lack of information, it was difficult to obtain average age of the patients. Many patients didn't have home and at the time of admission to the hospital,

**Table 1. Represents the relation of mortality and variables**

Variables	N(%)	Mortality [n (%)]	OR (IC 95%)	p-value
INR>1.6	20(39)	6(27)	1.79 (0.42-7.50)	0.203
AST/TGO (>6 times its normal value)	10(21)	1(9)	0.35 (0.02-2.89)	0.169
ALT/TGP (>6 times its normal value)	10(19)	2(12)	0.41(0.49-4.11)	0.251

some of the patients were suffered from mental illness. Many of the patients were expired (25%) before being identified by their relatives. 20 patients had international normalized ratio greater than 1.6, with total number of 6 fatalities (OR 1.79 with 95% IC of 0.42-7.50,  $p=0.203$ ) (as shown in table 1). Spearman's correlation coefficient was calculated positive (0.410).

Ten patients had AST levels 6 times larger than the normal value with mean of 580 U/L ( $p=0.175$ ). For AST levels and mortality, the spearman's correlation coefficients were very low (-0.018). The remaining ten patients had ALT six times larger than the normal value ranging from 17 to 19,140 U/L with mean value of 560 U/L ( $p=0.251$ ). For mortality and ALT levels the spearman's correlation coefficient was very low (-0.060). The center body temperature was recorded in the patients from 40 °C to 43.5 °C with a mean value of 43 °C.

## 5. CONCLUSION

In this research, an analytical study has been done successfully for the patients suffered from classic heat stroke. Mainly, the acute liver failure (ALF) or acute liver injury (ALI) can cause by classic heat stroke in the peoples who lived at warm places. During the hospital stay, patients who developed acute liver failure or acute liver injury had high level of risk of mortality. The study has been done on group of 58 male patients who hospitalized in government hospital during the summers. The mortality rate of 25% has been observed for this study. There are some weaknesses are also in this study due to the lack of information such as patients age and the two cohorts separated in time. Heat stroke is rare medical condition but it must be take care of by peoples who live at warm places.

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## CONSENT

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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