Fever in Trauma Patients: Evaluation of Risk Factors, Including Traumatic Brain Injury

By Victoria Bengualid, MD, Goutham Talari, MD, David Rubin, MD, Aiham Albaeni, MD, Ronald L. Ciubotaru, MD,† and Judith Berger, MD

Background The role of fever in trauma patients remains unclear. Fever occurs as a response to release of cytokines and prostaglandins by white blood cells. Many factors, including trauma, can trigger release of these factors.

Objectives To determine whether (1) fever in the first 48 hours is related to a favorable outcome in trauma patients and (2) fever is more common in patients with head trauma.

Method Retrospective study of trauma patients admitted to the intensive care unit for at least 2 days. Data were analyzed by using multivariate analysis.

Results Of 162 patients studied, 40% had fever during the first 48 hours. Febrile patients had higher mortality rates than did afebrile patients. When adjusted for severity of injuries, fever did not correlate with mortality. Neither the incidence of fever in the first 48 hours after admission to the intensive care unit nor the number of days febrile in the unit differed between patients with and patients without head trauma (traumatic brain injury). About 70% of febrile patients did not have a source found for their fever. Febrile patients without an identified source of infection had lower peak white blood cell counts, lower maximum body temperature, and higher minimum platelet counts than did febrile patients who had an infectious source identified. The most common infection was pneumonia.

Conclusions No relationship was found between the presence of fever during the first 48 hours and mortality. Patients with traumatic brain injury did not have a higher incidence of fever than did patients without traumatic brain injury. About 30% of febrile patients had an identifiable source of infection. Further studies are needed to understand the origin and role of fever in trauma patients. (American Journal of Critical Care. 2015; 24:e1-e5)
This article focuses on fever in trauma patients who are admitted to the intensive care unit (ICU) for at least 2 days. We examine 2 questions: (1) does fever in the first 48 hours portend a favorable outcome and (2) what is the impact of head trauma (traumatic brain injury [TBI]) on fever? The role of fever in trauma patients remains unclear. The following questions remain unanswered: Does fever represent a strong immune response and can it be used to predict a favorable outcome? Does fever have a role in minimizing bacterial invasion? Or does fever, by increasing metabolic rate and cardiac output, predispose patients to an increase in mortality or brain injury?

Several articles have examined the role of fever in ICU patients. Circiumaru et al. followed 100 patients admitted to the ICU in a tertiary care, inner city hospital. Fever was present in 70% of patients admitted to the ICU, was apparent early in the ICU course, and correlated with scores on the Acute Physiology and Chronic Health Evaluation (APACHE) II but not with mortality.

Young et al. examined fever in ICU patients with and without infections. Mortality decreased with increased peak temperatures in patients with infections, and mortality increased in patients without infection who had body temperatures greater than 39°C. A second study was conducted in surgical patients with bloodstream infections. Fever correlated with survival, but not with white blood cell (WBC) counts or type of pathogen. These studies suggest a protective effect of fever in patients with infections.

Studies have examined the impact of brain injury on fever and cytokine production in cerebrospinal fluid and blood. Cytokines can be both protective and damaging to the brain depending on the cytokine and the quantity produced. Rincon et al. conducted a retrospective study in patients with acute strokes, intracerebral hemorrhage, or TBI. About 59% of patients with neurological events had fevers develop, compared with 47% in patients without neurological problems (P=.007). Fever in these patients with brain injury was associated with increased mortality.

**Methods**

Trauma patients were identified by using the St Barnabas Hospital registry from 2008 to 2010. St Barnabas Hospital is a level 1 trauma center located in the Bronx, New York. Patients were included if they were age 15 years or older and admitted for at least 2 days to the ICU. Data were collected until discharge or up to 30 days.

Fever was defined as a body temperature of 100.4°F (38.0°C) or greater and was measured orally. Fever workup was based on clinical assessment and could include cultures of blood, sputum, urine, wound, or stool and a Clostridium difficile toxin assay. At the time of the study, patients with TBI were not undergoing a hypothermia protocol.

Patients were classified as having underlying medical conditions if those conditions predicated their trauma admission. Patients were counted as intubated except if they were intubated for a surgical procedure and immediately extubated. Procedures included all surgical procedures except those related to long-term care such as tracheotomy and feeding tubes.

We examined fever at 2 different time points: in the first 48 hours to see if fevers correlated with mortality and during the entire ICU stay to investigate if fever reflected infection and mortality. This study was approved by the hospital’s institutional review board.

**Statistical Analysis**

Groups were compared by using a χ² test. Means were compared by using an independent sample t test. Logistic regression was used for multivariate analysis, with 95% confidence intervals and Hosmer-Lemeshow goodness of fit. The threshold for significance is a P value of .05.

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**About the Authors**

Victoria Bengualid is the program director for internal medicine at St Barnabas Hospital, Bronx, New York. Goutham Talari is an internist at UK Healthcare, Lexington, Kentucky. David Rubin is director of pediatrics at St Barnabas Hospital. Aiham Albani is an assistant professor of medicine at Johns Hopkins Medicine, Baltimore, Maryland. Ronald L. Clubotaru (deceased) was director of medicine at St Barnabas Hospital. Judith Berger is chief of the division of infectious diseases at St Barnabas Hospital.

Corresponding author: Victoria Bengualid, MD, Department of Infectious Diseases, St Barnabas Hospital, 4422 Third Avenue, Bronx, NY 10457 (e-mail: vbengualid@sbhny.org).
Results

Demographics and Types of Trauma

For the 162 trauma patients who met the criteria for inclusion in the study, 31% of admissions were due to falls, 16% to motor vehicle accidents, 14% to being hit by a car as a pedestrian, 14% to stab wounds, 12% to assault, and 11% to gunshot wounds. The study group was predominantly male (81%), with a mean (SD) age of 42 (20) years. The mean (SD) for APACHE II score was 13 (8), for score on the Glasgow Coma Scale was 11 (4), and for the Injury Severity Score (ISS) was 17 (6).

Fever During the First 48 Hours

In order to determine if fever in the first 48 hours was a predictor of mortality, we divided all trauma patients into 2 groups: fever or no fever present in the first 48 hours after admission (Table 1).

Patients with fever had significantly lower scores on the Glasgow Coma Scale, higher APACHE II scores, and a higher ISS than did patients without fever. Patients with fever also differed in the number of underlying medical conditions, but no one specific underlying condition (diabetes, dialysis, or alcohol use) was identified as predisposing to fever. Mortality was greater in febrile than in nonfebrile patients. More febrile patients required intubation and had a surgical procedure (correlated specifically for craniotomy and burr holes). No difference in highest WBC count, highest body temperature, or lowest platelet count was apparent between patients with and without fever.

Table 2 shows the result of the multivariate analysis. Fever correlated with intubation and underlying medical conditions. Fever was not a predictor of mortality.

Source of Fever in the ICU

A total of 82 patients (51%) had fever at some point in their ICU stay. Patients who had a source found for their fever stayed longer in the ICU (mean [SD], 19 [28] days vs 7 [5] days; P = .02) and in the hospital (28 [32] days vs 13 [10] days; P = .01) than did febrile patients without an infectious source found.

Despite fever workup, no source of infection was found in most patients (n = 57, 70%). The ability to identify a source of infection did not differ among groups of patients with different risk factors, including TBI, intubation, or undergoing a surgical procedure (Table 3). Patients with an identifiable source for their fever, in contrast to patients where no source was found, had higher maximum body temperature, higher maximum
WBC count, and lower platelet counts. Table 3 shows the multivariate analysis where peak WBC count remained significantly higher in febrile patients with an identifiable source for their infection.

The most common infectious source was pneumonia (34%), followed by urinary tract infection (20%), wound infections (14%), abdominal source (14%), and *Clostridium difficile* (12%). Two patients had a deep vein thrombosis. The timing for an infection developing is illustrated in the Figure. Three-quarters of patients with pneumonia were intubated.

The yield of blood cultures was low. Of 341 sets sent, 11 (3%) showed growth of microorganisms. Four grew gram-negative organisms, 6 grew coagulase-negative *Staphylococcus*, and 1 grew an anaerobe.

**Impact of TBI on Mortality**

Patients with TBI compared with no TBI were older (mean [SD], 45 [21] years vs 38 [18] years; *P* = .02), had higher APACHE II scores (15 [7] vs 11 [8]; *P* = .03), and a higher ISS (18 [6] vs 15 [5]; *P* = .005). They were more likely to be intubated (61% vs .005), have a surgical procedure (66% vs .001), and die (70% vs .001). Age, blood transfusions, underlying medical disease, highest body temperature, highest WBC count, and lowest platelet count did not correlate with TBI. In a multivariate analysis, TBI correlated with mortality and undergoing a surgical procedure (Table 2).

In order to isolate the effect of TBI, patients with TBI were further divided into 2 groups as follows: those with TBI alone and those with TBI plus other injuries at other sites. The groups were similar except that more patients in the group with additional injuries had higher ISS, higher APACHE II scores, and had undergone surgery. The multivariate analysis revealed no significant differences between these 2 groups. The mortality in the group with TBI alone was 17%, compared with 30% mortality in the group with TBI plus other injuries (*P* = .18).

**Impact of TBI on Fever**

Fever in the first 48 hours did not differ between patients with or without TBI or between patients with TBI alone or TBI plus other injuries: 41% in TBI only, 53% in TBI plus other injuries, 27% in patients without TBI (*P* = .35). The number of days febrile did not differ between patients with or without TBI.

The source of fever was identified in 30% of febrile patients with TBI and in 35% of febrile patients without TBI (*P* = .67). The most common source of fever was pneumonia. This occurred in 12% of febrile patients with TBI and in 11% of febrile patients without TBI. The highest fever, the greatest WBC count, and the lowest platelet count did not differ between patients with and without TBI.

**Discussion**

Fever in the first 48 hours after trauma was not a predictor of dying or of not dying. Fever was seen more often in patients who were intubated, even after the data were adjusted for severity of injury. These results suggest that the "stress" of trauma as manifested by fever did not protect the patient from death. One limitation is that the stress response can manifest in ways other than fevers. Further studies
are needed to examine the roles of specific cytokine production after trauma and the roles that cytokines play in fever and survival.

The next question focused on the effect of TBI on fever and mortality. The patients with TBI were similar to the patients without TBI as far as developing fevers in the first 48 hours and the number of days febrile in the ICU. However, fever in TBI patients was not a predictor of mortality as Rincon et al had reported. Rincon et al, however, included patients with strokes and intracerebral hemorrhage in addition to TBI. They reported that fever on admission to the ICU was common and was independently associated with in-hospital mortality.

Our results highlight the difficulty in finding a source of fever in trauma patients admitted to the ICU. Other parameters of infection such as maximum WBC count, highest body temperature, and lowest platelet counts were seen more often in febrile patients with a source of infection than in febrile patients without a source found. Very few patients had a bacteremia, but we did not control for patients who clinically appeared to have sepsis. This finding suggests that infections are not the main reason for fever in these trauma patients. Other possible causes of fever such as the severity of injuries or undergoing surgery were not significant factors on multivariate analysis.

Limitations of this study include the retrospective nature of the study, the number of patients recruited, the lack of measurement of cytokines, and the inability to compare febrile and afebrile patients with infections (as there were too few infected patients). Many questions remain about the etiology of fever and its benefits in trauma patients.

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REFERENCES

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