Journal of Clinical and Translational Hepatology **2021** vol. 9(5) | 605–606
DOI: 10.14218/JCTH.2021.00307

Letter to the Editor

Characteristics and Outcome of Exertional Heatstroke Patients Complicated by Acute Hepatic Injury

Heewon Yang[1], HyukHoon Kim[2] and Sangchun Choi[2*]

[1]*Department of Emergency Medicine, Aerospace Medical Center, Cheong-ju, Republic of Korea;* [2]*Department of Emergency Medicine, Ajou University School of Medicine, Suwon, Republic of Korea*

Received: 27 July 2021 | **Revised:** 18 August 2021 | **Accepted:** 19 August 2021 | **Published:** 15 September 2021

Citation of this article: Yang H, Kim HH, Choi S. Characteristics and outcome of exertional heatstroke patients complicated by acute hepatic injury. J Clin Transl Hepatol 2021;9(5):605–606. doi: 10.14218/JCTH.2021.00307.

To the editor,

We have read the article titled "Characteristics and Outcome of Exertional Heatstroke Patients Complicated by Acute Hepatic Injury: A Cohort Study" by Ji *et al*.[1] We congratulate the authors for this insightful article. In this letter, we would like to raise several issues about the article to provide constructive criticisms.

Heatstroke involves a systemic inflammatory response, the full damage of which is not only limited to the hepatobiliary system. Instead, it can also cause damage to other organ systems, including the central nervous system, cardiovascular system, gastrointestinal system, hematological system, and immune system.[2] However, the authors do not seem to weigh multiple organ failure following heatstroke. This can be misleading to the readers, who may believe that development of acute liver failure (ALF) is common in patients with heatstroke. Bi *et al*.[3] reported that exertional heatstroke uncommonly progresses to ALF; therefore, ALF secondary to heatstroke is rare. Additionally, the authors define acute hepatic injury simply as a coagulopathy with the elevated international normalized ratio (INR), to which we cannot agree. Lack of sweat and impaired heat dissipation would represent hypovolemic conditions that increase blood viscosity and the risk of thrombosis leading to microvascular hypoperfusion.[4] During the coagulation response in heatstroke, hyperthermia typically occurs, damaging vascular endothelium and inducing microthrombosis and fibrin formation—the disseminated intravascular coagulation may clinically manifest.[5] Secondly, the authors seem to underestimate the significance of brain injury in the patients with severe heatstroke, evidenced by the use of the Glasgow Coma Scale only for evaluation in their study. According to Hifumi *et al*.,[2] brain injury in heatstroke can cause severe cerebral edema, an essential indicator of neurologic sequelae and death. Using an imaging modality, such as brain CT and MRI, should be considered for evaluating brain edema as a severity index of heatstroke.[6] Finally, we think that the criteria used for the infection group were inappropriate, i.e. procalcitonin elevation > 2 ng/mL and white blood cell count > 10×10^9 /L. Heatstroke is known as a systemic inflammatory syndrome that results in a sepsis-like condition.[7] The permeability of gastrointestinal epithelia may increase due to damaged tight junctions and cell membranes during the state of hyperthermia, splanchnic hypoperfusion, and hypoxia.[8] Subsequently, the barrier dysfunctions in the gastrointestinal tract tend to result in the translocation of bacterial endotoxin or complete microorganisms from the intestinal epithelium to the bloodstream that may favor the occurrence of a systemic inflammatory response.[9,10] These inflammatory mechanisms can lead to elevated serum procalcitonin levels in the patients but without evidence of bacterial infection.[11] However, among the typical heatstroke patients, the association between elevated serum procalcitonin level and bacterial infection is not clear. Therefore, the authors' criteria for the infection group are misleading in that elevated procalcitonin level alone does not indicate the infectious state and is not a risk factor for mortality in heatstroke.

We hope that our clarification would assist the readers in obtaining a correct understanding of the essential roles of the liver in the development of heatstroke.

Funding

None to declare.

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study design (SC, HK), drafting of the manuscript (HY), revision of the manuscript (SC, HY). All authors approved the final version of the manuscript.

References

[1] Ji J, Gao J, Wang C, Ouyang L, Liu Z, Liu Z, *et al*. Characteristics and outcome of exertional heatstroke patients complicated by acute hepatic injury: a cohort study. J Clin Transl Hepatol 2021;doi:10.14218/JCTH.2021.00084.

Abbreviations: ALF, acute liver failure.

[*]**Correspondence to:** Sangchun Choi, Department of Emergency Medicine, School of Medicine, Ajou University, 164 Worldcup-ro, Yeongtong-gu, Suwon 16499, Korea. ORCID: https://orcid.org/0000-0003-2271-3434. Tel: +82-31-219-7750, Fax: +82-31-219-7760, E-mail: avenue59@ajou.ac.kr

[2] Hifumi T, Kondo Y, Shimizu K, Miyake Y. Heat stroke. J Intensive Care 2018;6:30. doi:10.1186/s40560-018-0298-4.
[3] Bi X, Deising A, Frenette C. Acute liver failure from exertional heatstroke can result in excellent long-term survival with liver transplantation. Hepatology 2020;71(3):1122–1123. doi:10.1002/hep.30938.
[4] Hashim IA. Clinical biochemistry of hyperthermia. Ann Clin Biochem 2010;47(6):516–523. doi:10.1258/acb.2010.010186.
[5] Bouchama A, Knochel JP. Heat stroke. N Engl J Med 2002;346(25):1978–1988. doi:10.1056/NEJMra011089.
[6] Jung YS, Kim HH, Yang HW, Choi S. Targeted temperature management in patients with severe heatstroke: three case reports and treatment recommendations. Medicine (Baltimore) 2020;99(45):e23159. doi:10.1097/md.0000000000023159.
[7] Epstein Y, Roberts WO, Golan R, Heled Y, Sorkine P, Halpern P. Sepsis, septic shock, and fatal exertional heat stroke. Curr Sports Med Rep 2015;14(1):64–69. doi:10.1249/jsr.0000000000000112.
[8] Lambert GP. Role of gastrointestinal permeability in exertional heatstroke. Exerc Sport Sci Rev 2004;32(4):185–190. doi:10.1097/00003677-200410000-00011.
[9] Pires W, Veneroso CE, Wanner SP, Pacheco DAS, Vaz GC, Amorim FT, *et al*. Association between exercise-induced hyperthermia and intestinal permeability: a systematic review. Sports Med 2017;47(7):1389–1403. doi:10.1007/s40279-016-0654-2.
[10] Ramírez P, Martí V, de la Plata AM, Salinas G, Bonastre J, Ruano M. Bacterial translocation in heat stroke. Am J Emerg Med 2009;27(9):1168.e1–2. doi:10.1016/j.ajem.2008.11.025.
[11] Tau ME, Cocca M. Misleading serum procalcitonin elevation in heatstroke. Eur J Case Rep Intern Med 2017;4(8):000695. doi:10.12890/2017_000695.