The authors reply:

We appreciate the interest of Awasthi and Angurana (1) in our findings recently published in Pediatric Critical Care Medicine (2). We agree that according to the current definition criteria, hyperferritinemic sepsis and hemophagocytic syndrome or hemophagocytic lymphohistiocytosis (HLH) syndrome may have overlapping characteristics or may even represent different spectra of the same inflammatory process (3).

We constantly suspect the possibility of secondary HLH in our clinical practice. Since 2007 when Garcia et al (4) showed the association of hyperferritinemia with unfavorable outcomes in critical pediatric patients with sepsis, we have considered the diagnosis of secondary HLH, but as mentioned in our article (2), we have limited access to more specific tests in our setting. In addition, the focus of our study (2) was to document the association between low ferritin values and mortality in a sample of patients with a high prevalence of iron deficiency anemia, as suggested by Ghosh et al (5) in a previous study conducted in India. Regarding the comparison of ferritin with other inflammatory biomarkers, a second study by our group comparing C-reactive protein, lactate, and total leukocytes has already been completed and is in the submission process.

Based on our results, we agree with Awasthi and Angurana (1) that serum ferritin represents a useful prognostic marker at values below 500 ng/mL in low- and middle-income countries. The fact that the biomarker was collected routinely at admission (<48 hr) by the PICU is a strength of our study (2). In addition, this is a low-cost, widely available, and easy-to-interpret test. These characteristics are essential for a potential prognostic marker. Nevertheless, we argue that it is difficult to establish a universal cutoff value for predicting mortality. As an example, the study by Horvat et al (6) with children hospitalized for different causes in the United States led to their recommendation of a cutoff of 373 ng/mL for predicting mortality. The presumably lower prevalence of iron deficiency anemia in their sample and the fact that they measured ferritin at any stage of the disease were probably the causes of the high cutoff value. There are no studies with systematic collection of ferritin at different stages during the evolution of critical illness in pediatric patients, as is the case for C-reactive protein studies (7). Our study (2) has the advantage of assessing ferritin in the first 48 hours after admission, which is more relevant for prognostic purposes than a test collected at any time during hospitalization. Last, we agree that serum ferritin in critical pediatric patients remains as a topic that merits further investigation.

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Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children

To the Editor:

We would like to congratulate the panel of 49 experts (1) for the recently published “Surviving Sepsis Campaign International guidelines.” The authors provided 77 evidence-based statements on the resuscitation and management of children with sepsis or septic shock. Acute organ dysfunction is a defining characteristic of sepsis. Several organ dysfunctions such as cardiovascular, ventilatory, renal, and endocrine failure were fully addressed in the article by Weiss et al (1), recently published in Pediatric Critical Care Medicine. However, during sepsis, one of the first affected organs is the CNS (2). Therefore, we want to draw attention to acute brain dysfunction, which was not mentioned in the text, although it is frequent in patients with sepsis and still hugely underdiagnosed (2).