

elaborate a diagnostic composite score for HLH called H score (4). In our cohort, we considered this cut off to try to elaborate the etiological spectrum of patients with markedly elevated ferritin and estimate the probability of developing HLH. On the basis of our results in an inpatient setting, the most likely causes for an elevated ferritin are hematological malignancy, severe infection, iron overload, and chronic kidney disease. HLH was diagnosed in 14% of cases. These findings are different from literature data where liver injury and infections seems to be most predominant etiologies. This could be explained by recruitment bias. In fact, our center is a general hospital with local recruitment, compared to other cohorts from tertiary teaching hospitals or reference centers for oncology or liver disease. Nevertheless, we recorded more cases of HLH (3). In the subgroup of patients with ferritin above $6000 \mu\text{g L}^{-1}$, we recorded 90% of our HLH patients, suggesting that a higher threshold of serum ferritin would be more specific of HLH. In this subgroup, however, we reported patients with hematological malignancy (35%) and sepsis (20%) as well. We conclude that high ferritin level cannot be used as a screening tool for HLH diagnosis and should be integrated into the clinical picture of HLH including fever, cytopenia, and organomegalia. We assessed the H score in all patients and showed that the probability of developing HLH was superior to 90% in 17.3% of cases. Thus, there were probably 2 HLH patients misdiagnosed in our cohort. We recommend the use of H score in each clinical situation with ferritin above $6000 \mu\text{g L}^{-1}$ to help physicians not misdiagnose HLH. Markedly elevated ferritin levels are far more

likely to accompany non-rheumatologic diseases like infection, hematological malignancy and iron overload. This study demonstrated that high ferritin could be considered as a factor of poor prognosis and high level of mortality in patients with a level above $6000 \mu\text{g L}^{-1}$. Further larger studies are certainly needed to confirm this finding. In accordance with previously published data, our findings support the fact that having high cut off value of ferritin, as used in the H score, may predict more patients with HLH diagnosis (3, 6). The measurement can help support but not confirm this diagnosis. Despite the limitations inherent in a retrospective review, our cohort did not suffer from recruitment bias in comparison with those reported in tertiary academic hospitals where patients are referred for liver transplantation (2).

■ REFERENCES

1. Meyron-Holtz EG, Moshe-Belizowski S, Cohen LA. A possible role for secreted ferritin in tissue iron distribution. *J Neural Transm.* 2011; 118: 337-47.
2. Moore C Jr, Ormseth M, Fuchs H. Causes and significance of markedly elevated serum ferritin levels in an academic medical center. *J Clin Rheumatol.* 2013; 19: 324-8.
3. Schram AM, Campigotto F, Mullally A, et al. Marked hyperferritinemia does not predict for HLH in the adult population. *Blood.* 2015; 125: 1548-52.
4. Fardet L, Galicier L, Lambotte O, et al. Development and validation of the H Score, a score for the diagnosis of reactive hemophagocytic syndrome. *Arthritis Rheumatol.* 2014; 66: 2613-20.
5. Henter IL, Horne AC, Aricó M, et al. HLH-2004: diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer.* 2007; 48: 124-31.
6. Ota T. Hyperferritinemia and diseases. *J UOEH-D.* 2000; 22: 189-200.