Clinical Profile And Predictors Of Outcome Of Hemophagocytic Lymphohistiocytosis In Critically Ill Children Of A Tertiary Care Pediatric ICU

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Background: Hemophagocytic Lymphohistiocytosis (HLH) is a rare multisystem disorder where a diagnosis, underlying etiology and management remains a challenge for intensivists as the distinction between hyperferritinemic conditions in PICU is not clearly understood. HLH can either be genetic (primary) or triggered (secondary) due to infections, malignancy or autoimmune disorders. In this study we describe the clinical characteristics and predictors of mortality in our cohort of critically ill children with HLH of any etiology.

Methods: Single center, retrospective study of children aged 2 months–12 years admitted with HLH to tertiary care pediatric ICU of Advanced Pediatric Center, PGIMER, India from January 2012 to August 2017 (5 years). We analyzed the clinical, laboratory characteristics, intensive care need like ventilation, hemodynamic support and the specific treatment from our electronic medical record. Multivariate logistic regression was used to identify the predictors of outcome.

Results: Total of 26 patients of HLH were observed over a period of 5 years. All but one episode were diagnosed as secondary HLH and did not have risk factors for familial HLH. Nineteen (67.9%) were males with a median age of 6.83 years (IQR 3.47, 9.64) and median PRISM 3 of 16 (IQR 13.5, 23). The underlying etiology was diagnosed in 15 patients (53.57%). Scrub typhus (n=5, 17.9%) was the commonest followed by acute encephalitic syndromes (n=3), dengue (n=2) and juvenile idiopathic arthritis (n=2). Ten patients (37.5%) had sepsis of unknown etiology. Twenty one out of 28 episodes fulfilled HLH 2004 criteria with a median Hemoglobin of 8.55 gm/dl (IQR 6.27, 9.9), total leucocyte count of 7000/uL (IQR 2725, 15175), platelets of 45,000/uL (IQR 22750, 98750), triglyceride 362 mg/dL (IQR 278, 597), fibrinogen of 1.4 g/L (IQR 0.94, 1.92). Median serum ferritin in the cohort was 5238 ng/mL (IQR 4084, 44000). Nineteen patients underwent bone marrow examination out of which 16 had an evidence of hemophagocytosis. Fifteen received steroids and 7 received IVIG as treatment of HLH. Seventeen out of 26 patients died (65.3%). On univariate analysis among non-survivors vs survivors, PRISM 3 scores [23 (IQR 15, 28) vs 13 (IQR 8.5, 16); P=0.012], Vasoactive inotropes scores (97 vs 11.67; P=0.001), number of PRBC transfusion episodes [1.37 (IQR 1, 2) vs 0.33 (IQR 1, 2); P=0.008] and need for mechanical ventilation (100% vs 11.11%; P<0.001) were predictive of poor outcome. Organ involvement such as acute respiratory distress syndrome (57.89% vs 11.11%; P=0.039); disseminated intravascular coagulation (63.15% vs 22.22%; P=0.046) and septic shock (94.73% vs 11.11%; P<0.001) were higher among the non-survivors. On multivariate analysis, none of these parameters were predictive of mortality.

Conclusion: Secondary HLH due to acute infections in PICU is associated with high incidence of organ failures and mortality. Prospective studies are needed to determine the effect of treatment and predictors of outcome.