Prevalence, Mortality, and Healthcare Utilization in Hemophagocytic Lymphohistiocytosis Among Lymphoma Patients: Insights From the NIS Database

J. KUTCHER[1], **I. NUR**[1] , **S. THANNIR**[1], **A. KHALIFA**[1], **S. SINHA**[2]

1. The Brooklyn Hospital Center, Brooklyn, NY
2. The Mount Sinai Hospital, Manhattan, NY

INTRODUCTION

- HLH is a life-threatening hyperinflammatory syndrome; lymphoma is the most common malignant trigger in adults[1],[3]
- HLH is frequently missed or diagnosed late, and survival in malignancy-associated HLH is poor[1]
- Population-level data on the burden and healthcare impact of HLH among U.S. lymphoma patients remain limited

AIM

To evaluate the national prevalence, in-hospital mortality, illness severity, and healthcare utilization associated with HLH among hospitalized lymphoma patients in the United States, compared with lymphoma hospitalizations without HLH.

METHOD

- **Retrospective cross-sectional study** of the National Inpatient Sample, **2016-2022**, applying HCUP discharge weights, strata, and clustering
- Adult (≥18 years) **lymphoma** hospitalizations identified by ICD-10-CM codes, grouped by presence or absence of concurrent HLH
- **Primary outcome:** in-hospital mortality; **secondary outcomes:** LOS, total charges, and organ-support markers
- **Survey-weighted logistic regression** for binary outcomes; log-transformed linear models for LOS and charges, reported as adjusted percent differences
- Adjusted for demographics, payer, ZIP income, hospital factors, Elixhauser score, and disease-specific comorbidities; acute organ dysfunction excluded as a mediator

CONCLUSIONS

- **Among hospitalized lymphoma patients, concurrent HLH is associated with:**
- Nearly fivefold higher adjusted odds of in-hospital death (24.3% vs 5.9%; adjusted risk difference +15.4 percentage points)
- Higher adjusted odds of DIC, dialysis, vasopressor support, and mechanical ventilation
- 57.5% longer adjusted length of stay and 79.1% higher adjusted charges
- **These findings underscore the need for early recognition and targeted management of HLH in this population**[2]
- Further studies could evaluate whether protocolized HLH screening in lymphoma admissions improves outcomes

RESULTS

1,723,069
Weighted lymphoma hospitalizations
NIS, 2016-2022

4,855
With concurrent HLH
0.28% of lymphoma admissions

24.3%
In-hospital mortality with HLH
vs 5.9% without HLH

4.96×
Adjusted odds of death
95% CI 4.18-5.89

Table 1. Baseline characteristics

Characteristic	HLH	No HLH
Median age, y (IQR)	55 (38-66)	67 (57-76)
Female	34.5%	43.5%
White	56.2%	71.0%
Black / Hispanic	14.6% / 14.8%	9.9% / 9.7%
T/NK-cell lymphoma	26.1%	3.3%
Hodgkin lymphoma	13.7%	6.9%
Medicare as primary payer	27.7%	56.7%
Urban teaching hospital	93.2%	79.9%

aOR = adjusted odds ratio; DIC = disseminated intravascular coagulation; LOS = length of stay; pp = percentage points. Counts are survey-weighted; adjusted models used 343,814 unweighted discharges (965 with HLH). All estimates apply HCUP discharge weights, strata, and clustering, and are adjusted for age, sex, race/ethnicity, payer, ZIP income quartile, hospital region, bed size and teaching status, admission source, weekend admission, and Elixhauser score. Acute organ dysfunction variables were excluded as potential mediators. Adjusted predicted risks (Figure 2) derive from survey-weighted marginal standardization with bootstrapped 95% CIs. P values are FDR-corrected.

Figure 1. Adjusted odds of in-hospital outcomes with HLH

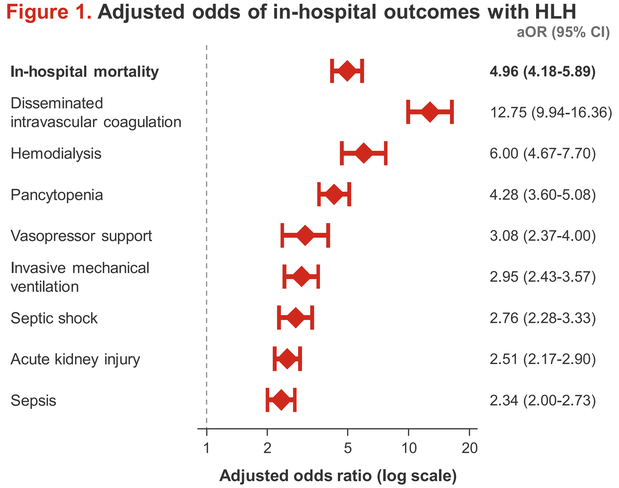

Figure 2. Adjusted predicted risk of in-hospital death

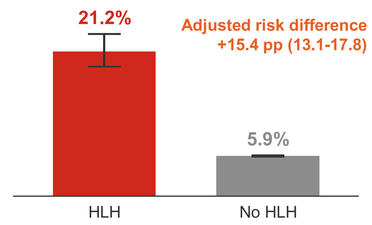

Table 2. Resource use

Measure	HLH	No HLH
Median LOS, days	10.0	5.0
Median charges	$145,512	$50,591

Adjusted difference: LOS +57.5% (48.8-66.8); total charges +79.1% (62.2-97.7)

LIMITATIONS

- HLH was identified by diagnosis codes alone, so the true prevalence is likely higher than 0.28%.
- No labs or bone marrow results were available to confirm the diagnosis.
- The NIS does not record lymphoma stage, treatment, or when HLH developed.

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CONTACT INFORMATION

Jonathan Kutcher, MD

Department of Internal Medicine, The Brooklyn Hospital Center, 121 DeKalb Avenue, Brooklyn, NY 11201

Email: **jkutcher@tbh.org**

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