Risk of Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic Syndrome in Lymphoma: A Real-World Comparison of Diffuse Large B-Cell Lymphoma and Follicular Lymphoma in Diabetic Patients

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Introduction

- Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic syndrome (HHS) are rare but carry **~10% inpatient mortality.**
- **DLBCL** (diffuse large B-cell lymphoma) is the most common aggressive lymphoma, treated with **R-CHOP regimens that contain high-dose corticosteroids**.
- **FL** (follicular lymphoma) is more indolent, typically treated with less steroid intensity.
- No prior study compared subtype-specific risks of diabetic emergencies in lymphoma.
- **Why this matters**: Even a +0.3% absolute increase in DKA translates to ~500 preventable ICU admissions per 100,000 diabetic lymphoma patients annually, with major cost and treatment delays.
- **Objective**: Compare risks of DKA and HHS in diabetic patients with DLBCL vs FL.

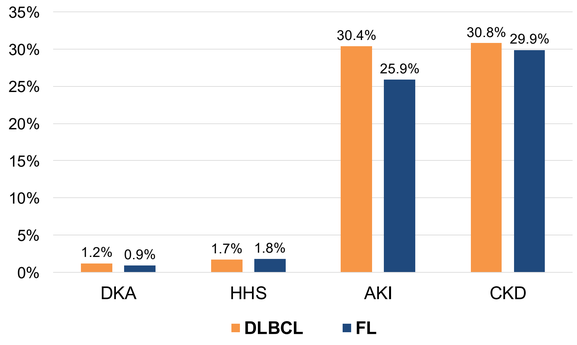
Methods

- **Data**: TriNetX Global Collaborative Network (143 sites).
- **Design**: Retrospective cohort, 2015–2025.
- **Cohorts**:
  - DLBCL: ICD-10 C83.3 + diabetes (E10., E11.)
  - FL: ICD-10 C82.* + diabetes (E10., E11.)
- **Outcomes**:
  - Primary: DKA (E10.1*, E11.1*), HHS (E10.0, E11.0) ≥1 day post-index
  - Secondary: AKI (N17.), CKD (N18.)
- **Analysis**: 1:1 propensity matching (age, sex, race, hypertension, obesity, cardiovascular disease, CKD).
- OR, absolute risk difference (ARD), 95% CI, p-values.
- **Limitations**: Prior outcomes not excluded; variable follow-up duration.
- **Ethics**: IRB-exempt.

Results

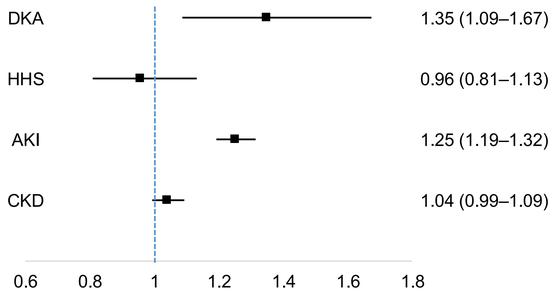
- Cohorts: 16,017 per arm; demographics and comorbidities balanced.
- **DKA**:
  - DLBCL 1.2% vs FL 0.9%
  - OR 1.35 (95% CI: 1.09–1.67), p=0.006
  - ARD: +0.3% → ≈500 preventable admissions annually
- **HHS**:
  - DLBCL 1.7% vs FL 1.8%
  - OR 0.96 (95% CI: 0.81–1.13), p=0.606
  - No difference
- **AKI**: OR 1.25 (95% CI: 1.17–1.33), ARD +4.5%, p<0.001
- **CKD**: OR 1.03 (95% CI: 0.97–1.10), NS

Figure 1: Absolute Risks of Outcomes Between DLBCL vs FL



Results Cont'd

Figure 2: Odds Ratio and 95% CI



Discussion

- **Finding**: DLBCL patients with diabetes had 35% higher odds of DKA vs FL.
- **Mechanism**: Steroid intensity of R-CHOP induction regimens likely drives acute insulin deficiency; HHS reflects different biology.
- **Why this matters**:
  - DKA = ICU admissions, treatment delays, higher cost, and worse survival.
  - Even modest ARD translates to a significant **national burden**.
  - This is the first evidence that diabetic emergencies differ by lymphoma subtype.
- **Guideline gap**: Current NCCN supportive care guidelines do not consider subtype-specific diabetes risk.
- **Practical step**: Daily glucose monitoring + early endocrinology referral for diabetic DLBCL patients.
- **Limitations**: EHR coding bias, unmeasured confounding, inclusion of prior outcomes.

Conclusion

- Diabetic patients with **DLBCL have higher DKA risk**; HHS risk similar to FL.
- **First-in-literature**, multi-institutional evidence of lymphoma subtype differences in diabetic emergencies.
- **Why this study is important**: Identifies a hidden, preventable source of morbidity, mortality, and cost in DLBCL care.
- **Action**: Supports proactive glucose monitoring and endocrinology referral in diabetic DLBCL patients.
- **Future direction**: Prospective studies to test preventive strategies and optimize treatment delivery.

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