Atypical Hemolytic Uremic Syndrome (aHUS) Clinical Characteristics and Treatment Patterns Associated with Readmission After Index Hospitalization

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Introduction

Atypical hemolytic uremic syndrome (aHUS) is associated with dysregulation of the alternative complement pathway and causes significant morbidity and mortality when undiagnosed or inappropriately treated. C5 inhibitors (C5i) improve thrombotic microangiopathy (TMA) response and renal recovery, but significant morbidity may remain. This study described the clinical characteristics and treatment patterns associated with readmission after index hospitalization using real-world evidence from one of the largest, most diverse cohorts of presumed incident aHUS in the United States (US).

Methods

This was a retrospective cohort study of 634 incident cases among hospitalized adult patients with presumed aHUS derived from the US Premier Healthcare Database, an electronic healthcare records database that contains ~25% of all US hospitalizations (January 1, 2011–June 30, 2021). aHUS was defined as the presence of an International Classification of Diseases (ICD)-9-CM/ICD-10-CM diagnostic code for TMA (446.6, M31.1, M31.10, M31.19) or HUS (283.11, D59.3) *and* a treatment code (standard charge, HCPCS, ICD-10-PCS) for a C5i, in the absence of a diagnostic code for secondary causes of TMA/HUS or other C5i indications. The proportion of patients readmitted following the index hospitalization was assessed at 30 days and 365 days following discharge, among other timepoints. The time from index hospitalization discharge to all-cause hospital readmission was defined as the number of days from the discharge date of the index hospitalization to the date of all-cause readmission. Readmission for aHUS was defined as a hospitalization lasting ≥2 days to avoid the inclusion of in-hospital infusion clinic visits for C5i treatment. Demographic and clinical characteristics were analyzed using a t-test, Wilcoxon rank test, Fisher's exact test, or Chi-squared test, as appropriate.

Results

Overall, 78/634 patients (12.3%) died during index hospitalization. Among the 556 patients who survived until discharge, 23.4% and 39.7% had a readmission within 30 days and 365 days, respectively. During the first 365 days, 20.1% of patients required multiple hospitalizations. The median time to first readmission was 27.5 days (interquartile range [IQR]: 9–102 days). Infection was a common cause of readmission (25.6%). Readmission within either 30 or 365 days was associated with longer median time between index admission and therapeutic plasmapheresis (TPE) (3 vs 2 days, p=0.0002, and 3 vs 2 days, p<0.0001, respectively), longer median time between index admission and C5i (10 vs 8 days, p=0.0441, and 10 vs 8 days, p=0.0005, respectively), and longer median time between index admission and renal replacement therapy (RRT; 4 vs 2 days, p=0.0030, and 3 vs 2 days, p=0.0053, respectively). Only readmission within 365 days was associated with median age (52 vs 46 years of age, p=0.0124) or a history of hypertension (80.5% vs 64.5%, p<0.0001), atrial fibrillation (9.5% vs 4.8%, p=0.0363), or heart failure (21.7% vs 14.6%, p=0.0395) at index hospitalization. Readmission within 30 or 365 days was not associated with sex, race, ethnicity, insurance type, geographical region, hospital size or location (rural vs urban), diabetes, chronic kidney disease, myocardial infarction history, TPE, TPE duration, corticosteroids (CS), CS duration, time to CS, RRT requirement, or TMA remission at discharge.

Conclusions

aHUS readmission rates remain high, despite treatment with C5i, and infection is a common cause of readmission. Delayed TPE, RRT, and C5i treatment for aHUS during index hospitalization, even if only for 1–2 days, were associated with increased readmission within 30 and 365 days. Future efforts should be made to examine the causal relationship between treatment delays and outcomes.