

Trends in Mucormycosis-Related Hospitalizations, United States, 2000–2013

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Background

- Mucormycosis is an invasive mold infection (IMI) that typically affects highly immunocompromised persons and is associated with substantial morbidity and mortality.
- Incidence of mucormycosis is particularly high among those with certain underlying conditions:
 - Hematopoietic stem cell transplant (HSCT)
 - Hematologic malignancy (HM)
 - Solid organ transplant (SOT)
- The burden of mucormycosis in the United States has not been well described.
- At least two factors may affect trends in mucormycosis:
 - Increase in number of susceptible persons
 - Use of voriconazole prophylaxis against invasive aspergillosis (IA)
- Primary objective:** Estimate nationally-representative incidence rates and trends in mucormycosis-related hospitalizations (M-RH) in the United States during 2000–2013.
- Secondary objective:** Compare trends in M-RH and IA-related hospitalization (IA-RH) among hospitalizations that were also related to higher-risk conditions including (HM, HSCT and SOT).

Methods

- Used data from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (HCUP), the largest database of publicly-available all-payer health care data in the United States.
- Inpatient Sample (NIS) is a nationally representative database of hospitalizations derived from billing data.
- National estimates are produced by assigning specific sampling weights to discharges based on hospital census region, rural/urban location, teaching status, bed size, and ownership.
- Used data from the United States Census Bureau to obtain denominators for the US population by year, age group, sex, race, and census region to calculate rates.
- International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9) diagnosis codes:
 - M-RH: 117.7
 - IA-RH: 117.3 and 484.6
 - HSCT V42.81, V42.82, and 996.85
 - HM: 200–208
 - SOT: V42.0, V42.1, V42.2, V42.6, V42.7, V42.83, V42.84, V42.89, V42.9, and 996.80–996.89 excluding 996.85
- We tested for linear trends in annual rates of overall M-RH and rates of M-RH and IA-RH occurring in conjunction with each underlying condition of interest using the weighted least-squares (WLS) technique.

Results

The estimated number of M-RH rose from 485 (95% CI: 363–607) in 2000 to 1,080 in 2013 (95% CI: 875–1,285). The overall rate of M-RH doubled from 1.7/million persons (95% CI: 1.3–2.2) in 2000 to 3.4 (95% CI: 2.7–4.1) in 2013 with an estimated APC of +5.2%. ($p < 0.001$).

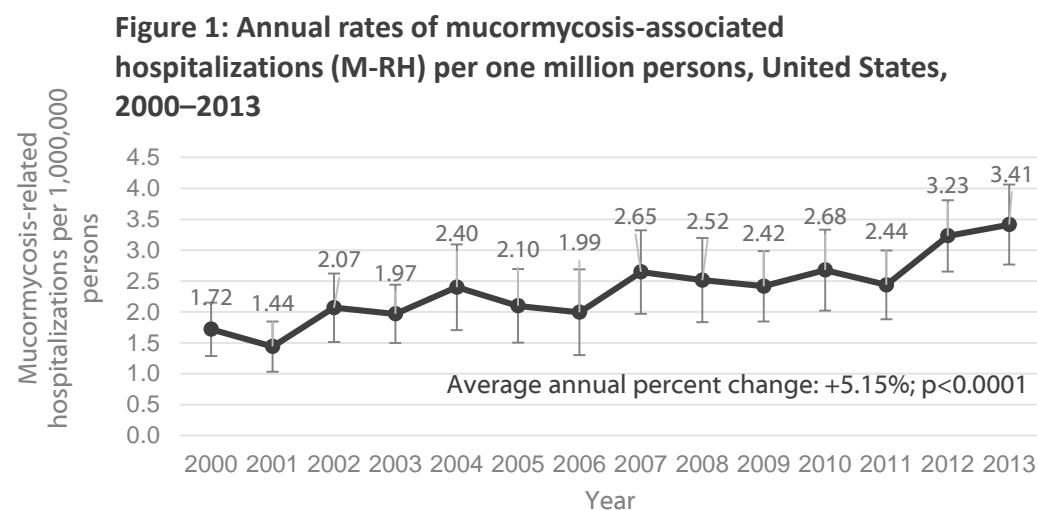
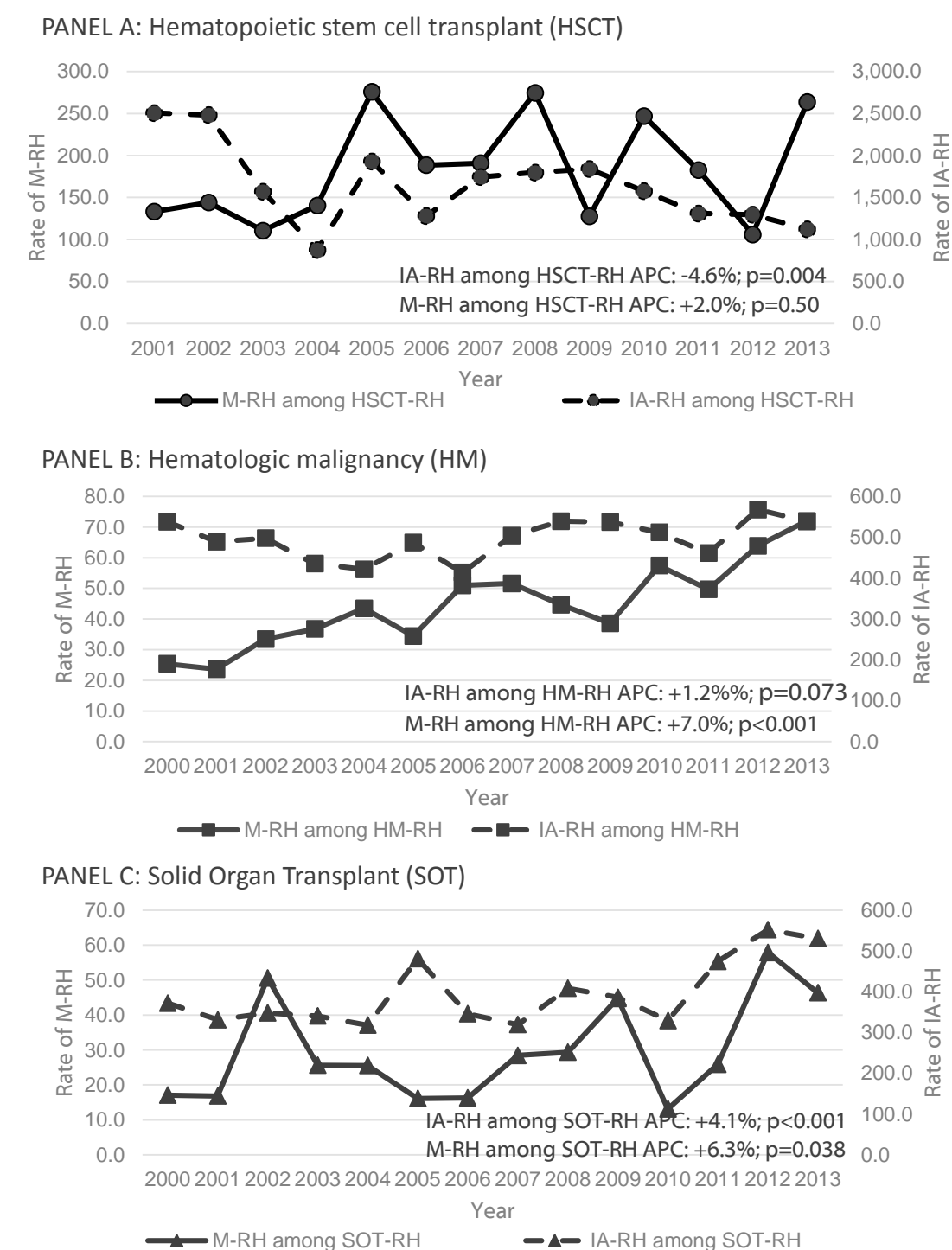


Table 1: Rates of mucormycosis-related hospitalizations by various demographic characteristics, United States, 2013

Characteristic	Rate per one million persons	95% Confidence Interval
Age group		
<18 years	1.5	0.6–2.4
18 to 44 years	1.7	1.1–2.2
45 to 64 years	5.5	4.3–6.8
≥65 years	7.2	4.9–9.4
Sex		
Male	4.4	3.4–5.4
Female	2.5	1.8–3.2
Race		
Black	3.4	2.1–4.7
Non-Black	3.1	2.4–3.7
Hospital region		
Northeast	1.5	0.6–2.4
Midwest	4.1	2.5–5.7
South	3.4	2.3–4.5
West	4.2	2.8–5.6

Figure 2: Annual rates of mucormycosis-related hospitalizations (M-RH) and invasive aspergillosis-related hospitalizations (IA-RH) per 100,000 hospitalizations for specific underlying conditions, United States, 2000–2013



Discussion/Conclusion

- The overall rate of M-RH doubled during 2000–2013
- Finding is consistent with reported increases in mucormycosis incidence from smaller studies of specific patient populations and data from other parts of the world.
- Because mucormycosis almost always requires hospitalization, the estimated 1,080 (CI: 875–1,285) M-RH in 2013 serves as a proxy for the current overall burden of these infections in the United States.
- Trends of IA-RH and M-RH differed by subgroup. Among hospitalizations related to
 - HSCT: IA-RH declined significantly whereas M-RH stayed stable.
 - HM: IA-RH stayed stable whereas M-RH increased significantly.
 - SOT: Both IA-RH and M-RH increased, but M-RH increased more than IA-RH.
- Declines or stability of IA-RH among patients with HM and HSCT could be attributed to use of voriconazole prophylaxis in these highly immunocompromised populations.
- Males had nearly 2-fold higher rates of M-RH among than females.
 - This finding has been previously reported with mucormycosis and male predominance has been noted in other fungal infections.
- M-RH rates in the northeast were substantially lower than other parts of the country.
 - Reasons could include variation in climate and ecology that may encourage mold growth, difference in distribution of underlying conditions such as diabetes, or regional differences in medical practices, including antifungal prophylaxis.
- Limitations include reliance on hospital discharge data, which is subject to misdiagnosis and errors in coding.
- Mucormycosis rates remain several fold lower than that of invasive aspergillosis, but mucormycosis is becoming an increasingly important IMI, especially among highly immunocompromised patients.
- Ongoing surveillance to better understand the true burden of mucormycosis is needed.

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