Reviewer's report

Title: Hospital days, hospitalization costs, and inpatient mortality among patients with mucormycosis: a retrospective analysis of U.S. hospital discharge data

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Reviewer: Sebastian Heimann

Reviewer's report:

The authors have performed an interesting and needed look at the outcomes among patients with mucormycosis. Data from a large US database (HCUP-NIS) were analyzed retrospectively with respect to hospitalization, costs and mortality. Furthermore, the manuscript is well written and the key-message is expressive.

Major Compulsory Revisions

Methods

1. The authors argue that identification of individuals was not (is not) possible. I have several concerns due to three main aspects: (i) mucormycosis is a very rare fungal infection, (ii) very detailed patient characteristics (e.g. age, sex, race, household income, payer type, underlying disease, comorbidities) were analyzed from the HCUP-NIS database and (iii) hospital characteristics (e.g. geographic region, urbanicity, teaching status, number of beds) could be analyzed, too. To my mind, the above mentioned aspects potentially allow an identification of human subject data. This raises the question of whether an ethic vote would be needed or not? This and the above mentioned aspects of potential identification of human subject data should be clarified in the methods section.

2. What was the reference time when group distribution of categories A-D was performed? At admission to hospital or during hospitalization? To my mind, in some circumstances, groups are not clear definable. For example, a patient who was severe immunocompromised due to neutropenia after chemo-therapy regimen or stem cell transplantation and an afterwards admission to intensive care unit (and the need of mechanical ventilation for >96h) could be categorized in group A or B. This should be clarified.

3. Are the calculated costs specifically attributed to mucormycosis? More precisely, are e.g. chemotherapy regimens excluded from cost calculation?

Results

1. A significantly longer LOS was analyzed when comparing the case vs. control group (mean= 16.5 days) resulting in mean excess costs of USD 64,526 for the case group. This means that additionally costs are approximately USD 4,000/day. My main feeling is that these additionally costs per day are higher than expected. Is it possible to make a more precisely cost analysis of the most
important cost drivers when treating a patient with mucormycosis? This would be most informative for the reader.

2. Table 2 & 3 and cost calculation in general: Analysis and calculation of costs and charges is very limited with respect to the main cost drivers or items with the lowest relevance of contribution to the total costs. What was the amount for the treatment on general ward, treatment on ICU, antimycotic respectively antiinfective treatment, diagnostic measures? This information is deeply interesting and should be added if possible.

Furthermore it is not clear what kind of costs were analyzed in the study. Were direct medical or non-medical costs included in cost calculation? This should be also clarified in the manuscript, too.

Discussion

1. In the last sentence of the discussion is written that “…this study likely underestimated the true burden of mucormycosis”. This could be true because e.g. indirect costs were not included in the analysis but caution is warranted because calculation of direct costs for the treatment of mucormycosis was possibly overrated due to the reasons as written in discussion (costs before onset of mucormycosis were potentially included in cost calculation).

Minor Essential Revisions

Methods

1. The type of health economic evaluation should be clarified in the method section. Is it a cost-of-illness analysis without calculation of indirect costs?

2. I have difficulties to understand the meaning of “number of discharge diagnoses” as written in the section of “study measures”. This should be clarified more precisely.

3. In the last sentence of “study measures” is written that “all costs and charges were adjusted to 2011”. What kind of adjustment was performed? Potentially a discounting due to the analyzed timeframe of 8 years? If so, what discount rate was used?

Results

1. Please indicate the percentage of African American and Hispanic in the second paragraph of the results.

2. I have difficulties to understand the meaning of “number of discharge diagnoses” and “number of procedures” as written in table 1. This should be clarified.

Discussion

1. In the last sentence of the second paragraph is written that “data are highly
generalizable as they represent the entire complement of the US acute care institutions.” What do the authors mean with “our data”? The clinical outcome, the calculated costs or both? This should be clarified. Furthermore, caution is warranted when comparing the results with other healthcare systems due to very different reimbursement or pricing systems.

Conclusion

1. Most information in this section is redundant with respect to the results and discussion (e.g. increase of hospital resource of 16 days and excess costs of USD 65,000).

Discretionary Revisions

Background

1. The following two references could be added in this section because they give a comprehensive overview of clinical data and treatment response of antimycotic therapy:


**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I have received research grants from Astellas, Gilead and MSD.