Reviewer's report

Title: Five-Years Surveillance of invasive Aspergillosis in a University Hospital

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Reviewer: Veli-Jukka Anttila

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Review of the submitted article: Five-Years Surveillance of invasive Aspergillosis in a University Hospital

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1. Is the question posed by the authors well defined?
The question of the article is clearly defined and is a clinical problem seen in tertiary hospitals overall.

2. Are the methods appropriate and well described?
The article is a retrospective analysis of patients with invasive aspergillosis during a five year period 2003-2007. The cases are classified by the appropriate and internationally acceptable criteria. Some terminology should be corrected.

1) Major Compulsory Revision:
In Methods section page 3 line 17 homologue stem cell/bone marrow transplantations? What does the homologue mean? Allogeneic or autologous stem cell/bone marrow transplantations. If both the number of each type of transplantation should be mentioned, because the risk of Aspergillosis is much higher after allogeneic than autologous stem cell transplantations. Does the number of the types of transplantations changed during the study period, because this could affect to the decreasing incidence of Aspergillosis in their hospital.

2) Discretionary Revision:
Do the study hospital follow their own transplantation patients? If they do not, the study hospital will not know the late infections seen in high risk patients?

3) Discretionary Revisions:
Is there HEPA filtrated/LAF rooms/wards in study hospital for high risk patients?
This should be mentioned.

It would be interesting to know, how many of the proven and probable cases are in SCT and organ transplantation patients early (up to 100 days after transplantation) and how many late (detected >100 days) after transplantation.

In page 4 line 17: nosocomial definition. I may be adequate definition; why not
“hospital acquired” or “health care associated”? The reference in line 19 in the
same chapter indicate to the article of Asciogly et al CID 2002. I could not find in
the article any mention about the nosocomial definition. The article classifies
aspergillosis to the proven, probable or possible (so called EORTC criteria). It is
not focusing at all to the origin aspergillosis (ie HAI or community acquired).

3. Are the data sound?

4) Minor Essential Revision:
The authors mentioned the possibility to investigate 234.095 cases during
2003-2007. Perhaps they mean that 234.095 patients were treated in their
hospital during their study period. Were they all inhospital patients or were there
also patients just visiting in policlinics? Perhaps they did not read exactly so
many patient records?

5) Minor Essential Revision:
In page 6 line 7: evaluation of risk factors? It is not risk factor but classification
according EORCT criteria. Could it be written: “Of 214 cases of IA were classified
56 (26%) as a proven etc.”

6) Major Compulsory Revisions:
In page 6 line 14-16: the number of organ transplantations should be given in
either in the text or in table 2. Number of different organ transplantations and the
risk of IA in each should be given in either in text or in table. After lung
transplantation there is a higher risk of IA than after other solid organ
transplantations. The reason for this could be related 1) The removed lungs
could be often colonized by aspergillus (for example often in CF patients) 2) the
immuno-suppression after lung transplantation is deeper than in other solid
transplantation 3) Lungs are directly in contact with environmental air 4) the ICU
period do last longer than after other transplantations and patients are more days
in ventilators 5) the air of cardiothoracic surgery ICU is contaminated with
moulds? Are the lung transplanted patients placed in HEPA filtered/ LAF rooms
in their postoperative period in mentioned ICU? Have you followed the quality of
Air in that ICU by any sampling method?

7) Minor Essential Revisions:
In page 7 line 12: cyclosporines? Why plural ? Should be calcineurin inhibitors or
ciclosporin/tacrolimus.
In table 2 : Haemopathy does mean haematological disease?

4. Does the manuscript adhere to the relevant standards for reporting and data
deposition?

8) Major Compulsory Revisions:
Table 2 need more data: number of every type of solid organ transplantation,
Haemopathy should be divided To allogeneic SCT, autologous SCT, treatment of
acute leukaemia and other. HIV could be deleted, because there were no cases.
Immunosuppressive treatment for systemic disease, could be just
immunosuppressive treatment.

Table 3: The title could be Classification of IA by microbiological sampling and data should be in more detailed form:

A) Culture positive
B) Just microscopic examination positive (direct microscopy or fungal staining)
c) Aspergillus antigenemia

BAL, BS and TS findings should be classified by same system ie. what type of mentioned microbiological finding were positive. If tracheal secretions and bronchial secretions were collected by similar way from intubated patients, they could be combined.

9) Minor Essential Revisions:
In page 7 line 21 As shown in Figure III: the figure is lacking.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

10) Minor Essential Revisions:
In discussion page 8 line 4: multimorbide term should be deleted.

11) Major Compulsory Revisions:
In page 9 in lines 11-14. the authors use the autopsy rate of whole country; do they have any autopsy rate numbers from their own hospital and even from the high risk patient groups such in patients died after organ transplantation or haematological unit. The use of overall autopsy rate in Germany is not valid for the study.

12) Minor Essential Revisions:
In page 9 in lines 28-29: solid malignancy tumors should be: solid organ malignancy tumors

13) Major Compulsory Revisions:
In page 10 lines 3-8: the authors compare their nosocomial IA numbers 1.85 % after organ transplantation and 0.97 % after SCT to all IA frequencies detected in specific types or organ and SCT transplantations. The comparison is not informative in this case. The comparisons should be done with similar cases (ie. just nosocomial cases in their material to nosocomial cases in published literature) and SCT cases should be divided to allogeneic and autologous cases).

14) Major Compulsory Revisions:
The authors did not discuss why they had a higher incidence of IA in years 2003 or 2004. They just mentioned that epidemiological and microbial data did not confirm an outbreak in February 2003 (Page 6 line 24). Outbreak of hospital acquired Aspergillosis are seldom detected in one month but can last several years in some epidemic outbreaks even over a year period. However, something had happen during the study period because of the incidence of IA decreased.
Where there construction works going on in their hospital in years 2003-2004 in high risk areas, did the clinicians change their prophylaxis after these years, or was there an change in hospital environment: new wards, ICU:s, air ventilation systems etc.

6. Are limitations of the work clearly stated?

As mentioned above, some limitations should be more clearly stated in discussion (the comparisons of nosocomial infection rates to all IA).

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?

Yes.

8. Do the title and abstract accurately convey what has been found?

15) Minor Compulsory Revisions:

In page 2 line 9-10: The number of proven or probable cases are 81, and this is not mentioned.

9. Is the writing acceptable?

As mentioned above some terms should be corrected.

I would advise the next step should be:

Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest:

An article whose findings are important to those with closely related research interests

Quality of written English

Needs some language corrections before being published

Statistical review

No, the manuscript does not need to be seen by a statistician.

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**Declaration of competing interests:**
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I declare that I have no competing interests