Reviewer’s report

Title: The persisting burden of invasive pneumococcal disease in HIV patients

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Reviewer: Francesca Montagnani

Reviewer’s report:

This observational study values retrospectively the burden of invasive pneumococcal diseases (IPD) in the last 10 years in a cohort of 1946 HIV patients in Calgary, Canada, in correlation with the use of pneumococcal polysaccharide vaccine (PPV-23).

The study has two main limitations, that can affect pneumococcal epidemiology, risk factors and incidence of IPD: geographical restriction and lack of antibody levels’ measurement.

However these remarks are well stated in the Discussion Section; besides, the question posed and discussed into the article is of relevant interest in HIV care and prophylaxis.

Nevertheless, major and minor revisions seem to be needed before a decision on publication can be reached.

Major Compulsory Revisions

ABSTRACT:

“The incidence of invasive pneumococcal disease (IPD) between 2000 and 2010 in a regional HIV population in Southern Alberta, Canada..” : the sentence is not fully correct since observation ends at 1st January 2010 and also Figure 1 refer till 2009. Please, better define and/or revalue the studied period, in all Sections of the article.

METHODS:

1) the authors should give a better definition of pneumococcal pneumonia since a pneumococcal aetiology can’t be diagnosed just by isolation from a sputum sample; the authors could differentiate e.g., a proved diagnosis from a presumptive/strongly suggested diagnosis (e.g. ref. to: DM Mushor Streptococcus pneumoniae; Chapter 200 in “Principle and Practice on Infectious Diseases”, Mandell, Douglas, Bennet Eds, 7th Edition). Moreover clinical, radiological and laboratory criteria to support the diagnosis of pneumococcal pneumonia should be added.

2) all risk factors for IPD - included into the analysis - should be listed and defined
3) in the nested case-control study other relevant analyzed variables should be stated (e.g. COPD, asthma and other relevant factors for pneumococcal infection)

RESULTS:
1) “There were 46 episodes of IPD; of these, 7 had positive sputum or BAL samples. There were 22 episodes of illness where S. pneumoniae was isolated from sputum or BAL only”: the kind of IPD and of “other” pneumococcal "illness" should be explained: e.g. bacteremic pneumonia? Meningitis? Non bacteremic pneumonia? Sinusitis? Otitis? It is known that pneumococcal vaccine doesn’t give a good protection for e.g. otitis
2) It could be relevant to report and analyze CD4 count and viremia during each single pneumococcal event and to insert these data into the multivariate analysis in Table 1
3) “Microbiology”: this Section is quite confusing and must be elucitated extensively. E.g. How many isolates were recovered from all pneumococcal diseases and from each single patients? How many isolates have been serotyped from sterile sites, from BAL and from other sites? How many strains have been serotyped in total: 50 or 55?
4) "Risk factors": this section should be clarified regarding significance of risk factors; identified risk factors are significant for what? IPD? Pneumonia? All pneumococcall diseases? Please, improve description of the regression and multivariate analysis.
5) Table 2 is cited in the text, but it is not present!
6) The relevance of the section “Hospitalization” should be pointed out and then discussed: e.g. why non invasive pneumococcal diseases required hospitalization?

Minor Essential Revisions

ABSTRACT:
1) “In 1946 HIV-patients with 11,099 years of follow up…”: did you mean “In 1946 HIV-patients with 11,099 persons/years of follow up”? Please check the term in abstract and in all Sections.
2) “COPD” abbreviation is not defined

RESULTS:
1) “The total number of days each patient was in “active care” at the clinic was measured from the initial visit until the patient moved, died, or was lost to follow-up”: please, better define the follow up period.
2) Add p values into Table 1
3) Figure 2: legend/title should report the source of isolates: as stated in Results
Section, those 50 strains were isolated just from sterile sites and BAL.

Discretionary Revisions
DISCUSSION:
1) apart from PCV-7, please discuss also regarding PCV-13. Is it already introduced into the paediatric vaccinal schedule in Calgary?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

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