Author's response to reviews

Title: Bacteremia in Hospitalized Patients With Human Immunodeficiency Virus: A Prospective, Cohort Study

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PDF covering letter
Response to Dr. Murri’s comments

1. The discussion section has been revised avoiding repetitions.
2. Discussion on etiologic agents has been shortened.
3. We have added in the discussion section explanations for differences from previous studies regarding the lack of association between bloodstream infection and injection drug use, CD4+ count, and neutropenia.
4. Health care providers’ and patients’ reluctance to openly discuss sexual history (including homosexual and heterosexual contact) may be responsible for the nonidentification of risk factors in 446 patients. We have added this fact in the revised manuscript.
5. Because of the inner-city location of our hospital, our patient population is predominantly African American. We have added this information in the methods section.
6. We have recognized the weakness of our study in that information about antiretroviral therapy and PCP prophylaxis are lacking. However, to determine the impact of HAART introduction on the bacteremia rate, we have reanalyzed our data and added in the results section the bacteremia rate for each year of the study period. Twenty-one of the 324 admissions (6%) during the first year of the study had bloodstream infection compared with 35 of 435 admission (8%) during the second year and 32 of 445 admissions (7%) during the third year ($P = 0.5748$). The mortality rate associated with bloodstream infection was the lowest during the last year of the study period.
7. We have added comments on survival difference between community-acquired and nosocomial bacteremia in the discussion section.
8. The numbers in line 4 of the results section of the abstract are “numbers,” not “%.”
9. We have deleted the sentence in page 3 starting with “The development….”
10. We have clarified the “place of acquisition.”
11. We have added the percentages in Table 5.

Response to Dr. Manfredi’s comments
1. We do not know how many of the patients were on HAART. However, to determine the impact of HAART introduction on the bacteremia rate, we have added in the results section the bacteremia rate for each year of the study period. Twenty-one of the 324 admissions (6%) during the first year of the study had blood stream infection compared to 35 of 435 admission (8%) during the second year and 32 of 445 admissions (7%) during the third year ($P = 0.5748$). We have also added the mortality associated with blood stream infection for each year of the study.
2. We agree with the reviewer’s comment that we did not include all risk factors for bacterial infection. We have acknowledged this in the discussion section.
3. We agree with the reviewer’s comment that reduced use of invasive procedures and shorter length of hospital stay may have contributed to the low incidence of catheter-associated bacteremia. We have added this in the discussion section.
4. The lack of association between the development of bacteremia and $CD4^+$ count may reflect the early stage of HIV infection in our patients. We have added this in the discussion section.
5. Most of the bacteremias were community acquired and the most common source of infection was pneumonia in our study. These facts may explain why *Streptococcus pneumoniae* and *Escherichia coli* were more
common that *Staphylococci* in the present study. We have added this explanation in the discussion section.

6. Thirty-four percent of the African Americans and 67% of the Hispanics had a history of injection drug use compared with 20% of the whites (*P* < 0.0001). We have added this in the results section. Because there were only a few Hispanics in the present study, the African Americans were more likely to be injection drug users than the whites, and the whites in the present study are not representative of the HIV-infected white population, the role of race may not be as significant as the statistics suggest. Compared with men, women were more likely to have heterosexual contact (28% vs. 8%) and less likely to have injection drug use (20% vs. 32%) as risk factors in the present study.

7. We agree with the reviewer’s comment that leukopenia is a risk for disseminated infection. The lack of association between bacteremia and leukopenia in the present study may reflect the earlier stage of HIV infection in our patient population. We have added this in the discussion section.

8. Using HIV-infected patients without blood stream infection as a control, our study showed that HIV-infected patients with blood stream infection had higher a mortality rate (18% vs. 4%). The first sentence of our conclusion is based on this finding.

9. We have reanalyzed our data dividing the study into 3 periods. Although the blood stream infection rates were similar, the mortality rate was the lowest during the third year of the study. The improvement in mortality may reflect the benefit from HAART. We have added this information in the results and discussion sections.

10. The sources of bacteremia are defined in the methods section of the revised manuscript.
11. To describe the role of HAART, we have reanalyzed our data as mentioned in response #9.
12. As per the reviewer’s suggestion, we have updated our references.
13. We have eliminated organisms such as *Corynebacterium* species, *Bacillus* species, *Propionibacterium* species, and unidentified Gram-positive rods from the revised manuscript. We do not have a good explanation for the lower rate of bacteremia in injection drug users. Analysis of our data shows that the median CD4$^+$ count for injection drug users was $0.08 \times 10^9$/L compared with $0.06 \times 10^9$/L for noninjection drug users ($P = 0.0042$). The earlier stage of the HIV infection in the injection drug users in our study may explain the lower bacteremia rate. We have added this in the revised manuscript.