

## Sepsis in People Living with HIV Infection: A Negligible Issue?

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### Editorial

The widespread use of combination antiretroviral therapy (cART) has substantially improved the prognosis of patients infected with HIV [1]. However, despite cART, HIV-infected patients are at greater risk of death compared to general uninfected population. As a consequence of the increase in survival, non-AIDS-related diseases now are a leading cause of death [2]. A large national cohort study from England and Wales found that AIDS- and non-AIDS related deaths accounted for 58% and 42% of cases, respectively. Furthermore, the analysis found that the mortality due to non-AIDS defining infections among HIV-infected patients is significantly higher than that of the general population (standardised mortality ratio 11; 95% confidence interval [CI] 9.8 to 12) [3].

HIV infection is associated with an increased risk of severe bacterial infections, including pneumonia, skin and soft tissue infections, and infective endocarditis [4-6]. However, few data have been published on the characteristics and outcome of sepsis in patients with HIV infection.

Overall, sepsis is associated with high morbidity and mortality in critically ill HIV-uninfected and HIV-infected patients [7,8]. In Euro SIDA cohort, sepsis in HIV-infected patients occurred at an incidence rate of 1.14 cases (95%CI 0.82 to 1.55) per 1000 person-years of follow-up (PYFU) with an increased risk in patients with advanced HIV disease (CD4+ cell count of <200 cells/ $\mu$ L) [9]. Sepsis accounts for a large share of critically ill HIV-positive patients admitted to the Intensive Care Units (ICUs) [10].

The etiology of sepsis in HIV-infected patients depends on many factors including age, CD4+ cell count, clinical setting (community-acquired [CA] or hospital-acquired [HA] infection) and geographic area (developed or developing countries) [11]. On this point, in a systematic review, Huson et al. found that non-typhoid salmonellae (36.6%), *Streptococcus pneumoniae* (30.4%), *Escherichia coli* (7.5%), and *Staphylococcus aureus* (7.0%) are the most common pathogens of CA-bacterial bloodstream infections in HIV-infected patients. Furthermore, compared to HIV-uninfected patients, HIV-infected patients had an increased risk to develop non-typhoid salmonellae

bloodstream infections (odds ratio [OR] 6.59; 95%CI 3.70 to 11.71). However, when are analyzed only the causative pathogens in adult HIV-infected patients living in developed countries, *S. pneumoniae* is the leading cause of sepsis accounting 22.8% of all isolates, followed by *S. aureus* (19.6%), *Salmonella spp.* (10.8%), and *E. coli* (10.5%) [12]. Moreover, over the last decade, methicillin-resistant *S. aureus* (MRSA) strains have emerged as serious pathogens in the nosocomial (HA-MRSA) and community (CA-MRSA) setting [13-15].

Septic HIV-infected patients admitted to the ICU have a worse prognosis than patients without HIV infection. On this point, Mrus et al. observed that HIV-infected patients admitted to the ICU for severe sepsis had an increased likelihood of death than HIV-uninfected patients (OR 2.41; 95%CI 2.23 to 2.61) [16]. Moreover, an observational study on critically ill patients admitted to the ICU showed that severe sepsis independently affected the short- and long-term mortality of HIV population (adjusted hazard ratios [HRs] for 30-day and 6-month mortality were 3.13 [95%CI 1.21 to 8.07] and 3.35 [95%CI 1.42 to 7.86], respectively) [8].

Finally, although debated by some authors, cART appears to be a major determinant of outcome in HIV-infected patients admitted to the ICU [17-19]. In a retrospective study Morquin, et al. found that the introduction of the cART in untreated patients is associated with a better long-term outcome (HR 0.166; 95%CI 0.043 to 0.642) [17]. Similarly Amancio, et al., in a observational cohort study including HIV-infected patients admitted to a Brazilian ICU, observed that cART is associated with a lower in-ICU mortality (OR 0.19; 95%CI 0.05 to 0.77) [18]. On the other hand, Meybeck no found benefit of cART on survival of HIV-infected patients, while observed that the administration of cART during ICU stay is associated with higher incidence of antiretroviral resistance after ICU stay [19]. In conclusion, despite the decrease in HIV-associated morbidity and mortality with the advent of cART, sepsis is yet a concern in HIV population. Further investigations to better characterize the role of cART as an independent prognostic factor for ICU survival are needed.

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