HIV and Critical Care Delivery in Resource-Constrained Settings

A Public Health Perspective

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The international acquired immunodeficiency syndrome (AIDS) community has largely focused its political, financial, and advocacy efforts on expanding early antiretroviral treatment to eligible individuals and preventing new infections in high-risk populations [1,2]. In resource-constrained settings, relatively little attention has been paid to the opposite side of the disease spectrum: the hospitalized human immunodeficiency virus (HIV) patient with advanced disease. Yet, despite progress in enrolling millions of people living with HIV (PLWH) into care in Sub-Saharan Africa, most individuals present with advanced disease [3]. Although the pursuit of an AIDS-free generation is essential, there remains an important parallel need to foster and maintain expertise in the clinical care of PLWH presenting with coinfections, including those requiring critical care. This paper reviews 3 important issues related to development of an acute care infrastructure for PLWH in resource-constrained settings from a public health perspective: 1) What are the priorities for improving critical care services for PLWH? 2) How will the evolving HIV epidemic—and particularly the increased burden of cardiovascular disease in this population—affect the future of critical care delivery in these settings? And, 3) what can the past 30 years of public health response to HIV teach us about developing a critical care health infrastructure in resource-constrained settings?

Although estimates of HIV prevalence in intensive care units in resource-constrained settings are lacking, general medical and surgical inpatient wards in Sub-Saharan Africa often report prevalence rates >50% [4,5], underscoring the need for high-quality inpatient HIV services in the region. Because management of HIV begins with an HIV diagnosis, among the greatest priorities is fostering a culture of provider-initiated testing for all inpatients [6]. Inpatient testing and linkage to outpatient care has been shown to be acceptable and feasible [7], whereas missed opportunities for testing undermine the quality of inpatient care and contribute to delays in outpatient treatment. Moreover, less than one-half of PLWH in Sub-Saharan Africa are aware of their status [8], so every medical encounter should be considered an opportunity to begin the cascade of linkage into care.

For those with a diagnosis, the impact of HIV infection on critical care is broad, and, though beyond the scope of this article, has been reviewed extensively elsewhere (Table 1) [9]. Key features of HIV-related critical care pertaining specifically to resource-limited settings include: optimizing the timing of antiretroviral therapy (ART) initiation, diagnosing and treating coinfections properly and promptly, and effective management of specialized AIDS-related clinical scenarios, including severe sepsis (from disseminated staphylococcal and streptococcal infections), intracranial hypertension (from cryptococcal meningitis), and respiratory failure (most commonly from *Pneumocystis jeroveci*, streptococcus, and tuberculosis infections). All of these conditions require advanced diagnostics, supportive care, and treatment, which may not be readily available in resource-constrained settings.

The complex nature of critical care of PLWH also requires multidisciplinary health professional expertise. In addition to physicians, expertise in nursing, pharmacy, physical therapy, and social work are essential to adequately monitor patients, manage dosing and drug-drug interactions, and ensure adequate attention to rehabilitation and end-of-life care. Importantly, with this package of multidisciplinary intensive care expertise, clinical outcomes for PLWH are similar to that of uninfected individuals [10,11]. These data support advocacy for acutely ill PLWH, to ensure that no patient is barred entry from an intensive care unit based on their HIV serostatus alone.

To ensure access to ART for acutely ill patients, collaborative relationships with outpatient providers, who are generally assigned responsibility to distribute ART medicines, should be developed and maintained. Data now strongly support early initiation of ART for the majority of PLWH, including those with most coinfections [12,13], and those receiving intensive care at the time of diagnosis [14]. Based on this evidence, intensive care units and other acute care settings should be empowered to initiate or restart ART for eligible patients. Building relationships between inpatient hospital providers and outpatient HIV clinics will be a prerequisite to coordinate and achieve this goal.

To best prioritize the resources for inpatient management of the 30 million PLWH worldwide, the evolution of the HIV epidemic must also be considered. Whereas opportunistic infections are currently the most common indication for hospitalization, continued successful expansion of ART is expected to spur an epidemiologic shift toward chronic disease. Evidence of this trend is already evident. Recent estimates in Sub-Saharan Africa, have demonstrated similar life expectancies for PLWH on ART and HIV-uninfected populations [15,16]. In

Dr. Siedner receives support from the National Institutes of Health (K23 MH099916). Dr. Siedner has no relationships that could be construed as a conflict of interest.

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GLOBAL HEART

VOL. 9, NO. 3, 2014
ISSN 2211-8160/$36.00.
http://dx.doi.org/10.1016/j.gheart.2014.08.006

TABLE 1. Considerations for critical care management of people living with HIV

Examples	HIV Coinfections	Noncommunicable Diseases
Diagnostics		
Basic laboratory testing	Metabolic disarray from sepsis, respiratory failure, acute hepatitis, drug toxicity; complete blood count testing for cytopenias, anemia, thrombocytopenia, and other hematologic abnormalities	Diabetic complications, cardiac ischemia, complications of malignancy (e.g., tumor lysis syndrome)
CD4+ T-lymphocyte testing by point-of-care or flow cytometry, HIV viral load and resistance testing	Coinfection risk, treatment monitoring, ART options	Malignancy risk, treatment monitoring
Gram stain and culture	*Staphylococcal*, *Streptococcal,* and other bacterial infections	N/A
Fungal stain and culture	Histoplasmosis, coccidiomycosis, cryptococcosis, and others	N/A
Cryptococcal antigen detection	Cryptococcal disease	N/A
Specialized staining	PCP testing	N/A
Viral PCR and culture	Herpes simplex virus, Varicella zoster virus, and others	N/A
Mycobacterial testing including molecular (e.g., Gene Xpert) and culture methods	Tuberculosis and nontuberculous mycobacterial infections (MAC)	N/A
Serologic testing	Viral hepatitis and other viral infections, toxoplasmosis	N/A
Stool testing	Soil transmitted helminths, cryptosporidium, microsporidium, and others	N/A
Imaging modalities, with preferential availability of ultrasound, x-ray, computed tomography with capability for angiography, and magnetic resonance imaging	Respiratory infections, intracranial infections	Myocardial infarction, congestive heart failure, cerebrovascular disease, diagnosis and complications of malignancy
Pathology	Multiple, including lymph node, bronchiolar lavage, lung, brain and other diagnostic biopsies	Malignancy diagnosis
Specialized clinical care		
Ventilator and respiratory failure management	Pneumonia most commonly from streptococcal infections, tuberculosis, PCP infections	Congestive heart failure, chronic obstructive pulmonary disease, asthma, and other forms of chronic lung disease
Shock	Most commonly streptococcal and staphylococcal-related sepsis	Cardiogenic shock
Neurologic intensive care	Cryptococcal meningitis, tuberculous meningitis	Cerebrovascular disease
Renal replacement therapy	Acute renal failure related to sepsis or drug toxicity	Acute and chronic renal failure from diabetes and hypertension complications
Liver failure management	Acute and chronic viral hepatitis, drug toxicity	Chronic liver disease related to alcohol use and nonalcoholic steatohepatitis
Ancillary services		
Pharmacy	Initiation, maintenance and discontinuation of appropriate ART regimens, drug-drug interactions most commonly from protease inhibitors, oral and intravenous administration routes, drug toxicity	Pharmacologic management of acute stroke and myocardial infarction
Nutrition	Critical care feeding, malnourishment management, drug-nutrition interactions	Diabetes, congestive heart failure, renal failure, liver failure, and other chronic disease nutrition issues
Occupational and physical rehabilitation care	Recovery from prolonged hospitalization, neurologic rehabilitation after meningitis or other intracranial infections	Recovery from automobile and other accidents, recovery from stroke, heart failure, and other
End-of-life care and hospice	Multiple	Multiple

ART, antiretroviral therapy; HIV, human immunodeficiency virus; MAC, mycobacterium avium-intracellulare complex; N/A, not applicable; PCP, *Pneumocystis jiroveci* pneumonia; PCR, polymerase chain reaction.