The sixth vital sign: HIV status assessment and severe illness triage in Uganda

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Setting: Four in-patient health facilities in western Uganda.

Objective: To determine the impact of an innovative multi-modal quality improvement program on human immunodeficiency virus (HIV) status assessment and the impact of HIV status on severe illness conditions and mortality.

Design: This was a staggered, pre-post quasi-experimental study designed to assess a multi-modal intervention (collaborative improvement meetings, audit and feedback, clinical mentoring) for improving quality of care following formal training in the management of severe illness in low-income settings.

Results: From August 2014 to May 2015, 5759 patients were hospitalized, of whom 2451 (42.6%) had their HIV status assessed; 395 (16.1%) were HIV-infected. HIV-infected patients were significantly more likely to meet criteria for shock (27.5% vs. 15.1%, risk ratio [RR] 1.8, 95% confidence interval [CI] 1.7–1.9, $P < 0.001$) and severe respiratory distress (6.7% vs. 4.3%, RR 1.5, 95%CI 1.2–2.0, $P < 0.001$), and were significantly more likely to die in hospital (12.0% vs. 2.9%, RR 4.1, 95%CI 3.2–5.4, $P < 0.001$). There was no evidence of improved HIV status assessment during the intervention period (36.5% vs. 44.8%, +8.3%, 95%CI –8.3 to 24.8, $P = 0.33$).

Conclusions: Hospitalized HIV-infected patients in western Uganda are at high risk for severe illness and death. Novel quality improvement strategies are needed to enhance hospital-based HIV testing in high-burden settings.

In settings of high human immunodeficiency virus (HIV) burden, assessment of HIV status is an essential component of severe illness management, both to guide empiric anti-microbial therapy against opportunistic pathogens and to inform the diagnosis, prognosis and management of HIV-infected patients presenting with severe infection.^{1–4} In such settings, hospital-based assessment of HIV status also provides an opportunity to provide an HIV diagnosis for patients previously unaware of their serostatus who otherwise have limited access to the health system.^{5,6}

In this context, the World Health Organization (WHO), through its Integrated Management of Adolescent and Adult Illness (IMAI) District Clinician Manual, recommends assessment of HIV status for all hospitalized patients in high HIV burden settings.⁷ This guidance is emphasized for severely ill hospitalized patients whose manifestations of shock, sepsis and severe respiratory distress may result from under-

lying HIV infection.⁷ Despite these recommendations, available data suggest that HIV status assessment among hospitalized patients in sub-Saharan Africa remains sub-optimal and inconsistent.^{5,8}

To strengthen the impact of the IMAI guidelines on severe illness management in Uganda, the Uganda-based non-governmental organization Walimu developed the Severe Illness Management System (SIMS) platform, a multi-modal, quality improvement program using a theory-informed approach to implementation. In the context of a larger intervention conducted to improve the management of severe illness, the objective of this study was to assess the impact of SIMS on HIV status assessment, as well as the impact of HIV status on severe illness conditions and mortality among adolescents and adults hospitalized in western Uganda.

STUDY POPULATION, DESIGN AND METHODS

Study sites and participants

The SIMS platform was introduced during the roll-out of the IMAI training program on severe illness to eight health facilities in western Uganda chosen by the Uganda Ministry of Health. Among these facilities, we selected three general hospitals and one in-patient community health center as study sites, primarily due to the availability of logistical support for training and ongoing quality improvement activities (Table 1). The district where these health facilities are located has a population of roughly 695 000, HIV prevalence is approximately 4% and antiretroviral therapy (ART) services are available at seven health facilities.^{9,10} At each site, we analyzed the data of consecutive patients aged ≥ 14 years admitted to the general medical wards, excluding those with emergent surgical or obstetrical conditions.

District clinician manual-based training and SIMS intervention

The core component of the severe illness training program is a 1-week instructional course on the IMAI district clinician manual's 'Quick Check' triage tool. The course, entitled Quick Check+, was developed for clinicians in resource-limited hospitals and features training in the early recognition of undifferentiated shock, sepsis, severe respiratory distress and altered mental status (Table 2). In this context, the course teaches a systematic approach to diagnosis and management: 1) rapidly obtain vital signs (temperature, blood pressure,

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TABLE 1 Characteristics of in-patient health facilities participating in SIMS intervention

Facility	Administration	In-patient beds available <i>n</i>	In-patient admissions per year* <i>n</i>	Out-patient visits per year* <i>n</i>
Health Facility 1	MoH	110	13 783	72 110
Health Facility 2	Private charity	272	8 814	47 094
Health Facility 3	MoH, private charity	205	10 851	24 645
Health Facility 4	Private charity	90	3 565	10 123

*Representative of data from 2013–2014.

SIMS = Severe Illness Management System; MoH = Ministry of Health.

etc.); 2) give first-line emergency treatment (oxygen, intravenous fluids); 3) assess HIV status; 4) classify severe illness conditions and develop emergent differential diagnoses; 5) give additional targeted treatments; and 6) perform further investigations.¹¹

To enhance the impact of the Quick Check+ training program, we designed the SIMS platform, a two-phase, multi-modal approach to implementation, using the ‘capability, opportunity, and motivation determine behavior’ (COM-B) model.¹² Before introducing SIMS, two program managers—including a medical doctor and a former hospital administrator, both with training in quality improvement strategies—worked with staff at each site to identify barriers to diagnosing and managing severe illness. During the SIMS training phase, staff at each facility developed a site-specific plan for quality improvement to address identified barriers. In the post-training reinforcement phase, three key behavior-change interventions derived from the COM-B model were planned using a ‘plan–do–study–act’ reinforcement cycle.¹³ These interventions included twice-monthly collaborative improvement meetings during which program managers worked with facility staff to implement and refine the quality improvement plan, continuous audits and reports of clinical performance (including HIV status assessment) conveyed to clinicians via weekly text messages and e-mails, and monthly clinical mentoring and simulation sessions led by an expert in severe illness care. During the collaborative improvement meetings, SIMS program managers worked with hospital staff (clinical officers and nurses) to review recent data audit reports and the previous meeting’s action plan.

This was followed by the creation of a new action plan to be pursued during the next ‘do’ cycle.

Staggered pre-post quasi-experimental study design

Before initiating data collection, we invited two clinical officers and two nurses, as well as two managers and two support staff from each site, to attend Quick Check+ training. We then implemented the SIMS platform using a quasi-experimental staggered pre-post design. We chose this design for ethical and logistical reasons, not wanting to withhold the SIMS platform, given its potential benefits for improving severe illness care to the level of WHO-recommended standards. Because we lacked the human capacity to implement SIMS at all sites simultaneously, however, we randomly assigned the sequence for introducing the SIMS interventions, with a new site launching approximately every 6 weeks and an a priori plan to launch two physically adjacent sites simultaneously (Figure 1) for convenience. Sites were randomized using a concealed, computer-generated random sequence for the four sites that was prepared by the data manager (EG) and revealed by one of the program directors (NKM) at the end of the Quick Check+ training in the presence of representatives from each site.

Data collection

Demographic, clinical, and in-hospital outcome data (mortality) were collected by clinical study staff through daily review of medical charts. HIV infection status was abstracted by clinical study staff at the time of hospital admission and discharge based on chart documentation of the patient being HIV-positive or

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Previous presentations of data: some of the results of this study have been previously reported in the form of an abstract at the 9th Annual Conference on the Science of Dissemination and Implementation in Health, 14–15 December 2016, Washington, DC, USA. Conflicts of interest: none declared.

TABLE 2 Diagnostic criteria for severe illness conditions covered in the Quick Check+ training program, as defined by the WHO District Clinician Manual

Condition	Diagnostic criteria
Shock	Systolic blood pressure ≤ 90 mmHg or heart rate ≥ 110 beats/min
Sepsis	Presumed infection (based on admission diagnosis*) and at least one of the following: – respiratory rate ≥ 24 breaths/min – heart rate ≥ 100 beats/min – temperature $\leq 36^\circ$ or $\geq 38^\circ$ Celsius
Severe respiratory distress	SpO ₂ $< 90\%$ or respiratory rate > 30 breaths/min
Altered consciousness	Abnormal AVPU score: responds to voice, responds to pain, or unresponsive

*Presumed infection based on clinician admitting diagnoses of amoebiasis, cholecystitis, colitis, diverticulitis, esophagitis, gastroenteritis, malaria, meningitis, pelvic inflammatory disease, pneumonia, tuberculosis, urinary tract infection.

WHO = World Health Organization; mmHg = millimeter of mercury; min = minute; SpO₂ = oxyhemoglobin saturation by pulse oximetry; AVPU = alert, voice, pain, unresponsive.

-negative. The method by which HIV status was determined (patient self-report and/or in-hospital testing) was not recorded. Data were double-entered into standardized forms on electronic tablets (CommCare, Dimagi, Cambridge, MA, USA), validated, and uploaded to a secure server in a format approved by the Uganda Ministry of Health (DHIS2, Oslo, Norway).

Data analysis

We used Poisson models with robust standard errors, adjusting for site as a fixed effect, to contrast the pre- and post-intervention frequency of HIV status assessment, then calculated marginal rate differences with 95% confidence intervals (CI) using standardization.¹⁴ We also used this approach to estimate the effect of HIV status on the frequency of severe illness conditions and mortality, controlling for period. All analyses were conducted using Stata v. 14 (StataCorp, College Station, TX, USA).

Ethical approval

The study was approved by the ethics committees at Makerere University School of Public Health (Kampala, Uganda), Uganda National Council for Science and Technology (Kampala, Uganda), University of California San Francisco (San Francisco, CA, USA) and Yale University (New Haven, CT, USA). The requirement to obtain individual informed consent was waived because the study was part of government-sponsored quality improvement activities and patient data were anonymized for analysis.

RESULTS

Study population characteristics

We analyzed data from 5759 patients admitted to medical wards across all four health facilities between 1 August 2014 and 31 May 2015 (Figure 2). Of these patients, 1633 (28.9%) were admitted during the pre-intervention period and 4126 (71.1%) during the intervention period. Between the pre- and post-intervention periods, there was no difference in median age (38 years, interquartile range [IQR] 24–55 vs. 37 years, IQR 23–58, $P = 0.95$) or female sex

FIGURE 1 Staggered pre-post quasi-experimental study design utilized for implementation of the SIMS intervention, August 2014–May 2015. Baseline period indicates time period following Quick Check+ training and before SIMS intervention. Other than provision of physical copies of the District Clinician Manual, no other form of post-training support was provided at the study sites during the baseline period. Intervention period indicates time period during which the SIMS intervention was implemented. SIMS = Severe Illness Management System.

FIGURE 2 Flow diagram for study. HIV = human immunodeficiency virus.

(58.9% vs. 57.4%, $P = 0.32$) of the admitted patients. Admission diagnoses, determined by the admitting clinicians, were similar in the pre- and post-intervention periods, with malaria (34.1% vs. 37.0%, $P = 0.05$), peptic ulcer disease (10.1% vs. 11.3%, $P = 0.33$), and severe hypertension (8.1% vs. 6.8%, $P = 0.08$) the most commonly recorded conditions.

SIMS implementation

The SIMS platform was implemented across the study sites as designed, with only a few adaptations. Originally scheduled to occur twice monthly, the collaborative improvement meetings took place on a monthly basis at each site. The meetings revealed two main barriers to consistent HIV testing: limited awareness by staff

FIGURE 3 Changes in assessment of HIV serostatus over study period, stratified by health facility. Zero on horizontal axis refers to time of initiation of SIMS intervention. HIV = human immunodeficiency virus; SIMS = Severe Illness Management System.

as to the location and quantities of HIV testing kits, and limited understanding of the importance of prompt HIV status assessment in severe illness management. Clinical mentoring sessions, originally scheduled to occur monthly, took place every 4–6 months at each site. Audit and feedback reports were implemented weekly as originally scheduled.

HIV status assessment

Among 5759 patients admitted during the study period, 2451 (42.6%) had their HIV status assessed during hospitalization (Figure 2). Of these, 395 were HIV-positive (16.1%), 116/560 (20.7%) in the pre-intervention period and 279/1891 (14.8%) in the intervention period. Compared to the pre-intervention period, there was a non-significant trend towards improvement in HIV status assessment during the intervention period (36.5% vs. 44.8%, +8.3%, 95%CI –8.3 to 24.8%, $P = 0.33$) (Figure 3). Significant improvement was observed at Health Facility 1 (26.2% vs. 46.5%,

+20.3%, 95%CI 15.1–25.4, $P < 0.001$), while Health Facility 2 showed no evidence of improvement (56.4% vs. 63.1%, +6.7%, 95%CI –8 to 21, $P = 0.37$). No improvement was observed at Health Facility 3 (40.6% vs. 37.5%, –2.9%, 95%CI –8.8 to 2.7, $P = 0.31$) or Health Facility 4 (27.7% vs. 23.0%, –4.6%, 95%CI –16.8 to 7.5, $P = 0.45$) (Figure 3).

Severe illness conditions and in-hospital mortality

Compared to non-HIV-infected patients, those with HIV infection were significantly more likely to meet the criteria for shock and severe respiratory distress (Table 3). Of 2333 patients with data available on HIV and vital status, 98 (4.2%) died in the hospital. Compared to non-HIV-infected patients, in-hospital mortality was significantly higher among HIV-infected patients (12.0% vs. 2.9%, risk ratio [RR] 4.1, 95%CI 3.1–5.38, $P < 0.001$) (Table 3).

DISCUSSION

We evaluated the impact of a novel quality improvement strategy on HIV status assessment and the impact of HIV status on severe illness conditions and mortality among adolescents and adults hospitalized in western Uganda. Despite regular access to ART services, the majority (57%) of the patients did not have their HIV status assessed. Those with HIV infection recorded were at high risk for severe illness and death. Given the expansive microbiological differential diagnosis and the benefits of targeted antimicrobial treatment strategies for HIV-associated severe illness, our findings support the need for continued development and evaluation of quality improvement interventions to enhance hospital-based HIV testing and emergency care in high HIV burden settings.

HIV-infected patients were significantly more likely to meet the criteria for key severe illness conditions and to die in hospital. In sub-Saharan Africa, the burden of acute, severe illness remains concentrated among HIV-infected patients, primarily due to severe infections and delayed hospital presentation.^{3,4,15,16} Traditionally, investments in HIV-related services in sub-Saharan Africa have focused on strengthening prevention activities and out-patient ART delivery.^{15,17,18} Given the high burden of severe illness

TABLE 3 Impact of HIV infection status on frequency of severe illness and overall and syndrome-specific in-hospital mortality*

Severe illness condition	HIV-positive (<i>n</i> = 395) %	HIV-negative (<i>n</i> = 2056) %	RR (95%CI)	<i>P</i> value
Frequency of diagnosis				
Sepsis	5.9	4.4	1.3 (0.9–2.0)	0.15
Severe respiratory distress	6.7	4.3	1.5 (1.2–2.0)	0.001
Shock	27.5	15.1	1.8 (1.7–1.9)	<0.001
Altered mental status†	4.0	3.1	1.3 (0.9–1.9)	0.16
Any severe illness condition‡	35.0	21.6	1.6 (1.4–1.9)	<0.001
In-hospital mortality	12.0	2.9	4.1 (3.2–5.4)	<0.001
Sepsis	—§	3.3	—	—
Severe respiratory distress	30.0	13.9	2.2 (1.2–3.9)	0.010
Shock	12.5	5.2	2.4 (1.3–4.3)	0.005
Altered mental status†	25.7	10.8	2.4 (1.0–5.4)	0.041
Any severe illness condition‡	14.7	6.2	2.4 (1.6–3.5)	<0.001

*Adjusted for site and includes only patients with recorded HIV infection status. HIV infection status was recorded by study staff based on chart documentation of the patient being HIV-positive or -negative. The method by which HIV status was determined (self-report and/or in-hospital testing) was not recorded.

†Defined as anything less than alert on the AVPU scale: alert (A), responsive to verbal stimuli (V), responsive to painful stimuli (P), unresponsive (U).

‡Defined as meeting criteria for ≥1 severe illness conditions (sepsis, severe respiratory distress, shock, altered mental status).

§No deaths reported among HIV-positive patients with sepsis.

HIV = human immunodeficiency virus; RR = risk ratio; CI = confidence interval; AVPU = alert, voice, pain, unresponsive.

and the demonstrated benefits of low-cost, high-impact interventions (i.e., early empiric antimicrobial therapy, fluid resuscitation, and vigilant monitoring), enhanced triage and protocolized emergency management is needed to improve hospital care in high HIV-burden settings.^{19,20} Improvements in hospital-based HIV care may also enhance confidence and engagement in HIV out-patient services.^{16,21,22}

In sub-Saharan African settings where HIV and tuberculosis (TB) co-infection is highly prevalent, the importance of HIV status assessment in severe illness management cannot be overemphasized. In line with evidence suggesting that survival for severely ill patients with HIV-associated TB is improved by early, empiric anti-tuberculosis treatment, the WHO currently recommends empiric treatment for HIV-infected possible TB patients with deranged physiologic parameters.^{23–26} Diagnostically, the urine-based lateral-flow lipoarabinomannan assay, a promising rapid diagnostic test for TB, demonstrates optimal performance in the setting of advanced HIV-related immunosuppression, and was recently endorsed by the WHO for use among HIV-infected patients with severe illness.^{27,28} These recommendations reinforce the importance of prompt assessment of HIV status, alongside the collection of physiologic parameters, in the triage of hospitalized patients in high HIV-burden settings.

In sub-Saharan African settings such as Uganda, where opt-out in-patient HIV testing is recommended by the Ministry of Health, studies have shown that implementation of provider-initiated counseling and testing (PICT) is inconsistent and sub-optimal.^{5,6,16,29–33} In the context of a larger quality improvement intervention, we observed a low frequency of HIV status assessment. During collaborative improvement meetings, health care workers identified barriers (i.e., limited awareness of testing kit supplies and the importance of HIV status in severe illness management) that have been previously reported in studies of PICT in the region.^{33,34} As the SIMS intervention was rolled out consistently at each site, the low frequency of HIV status assessment reinforces the importance of continued assessment and intervention on context-specific barriers to foster sustained improvements in implementation.³⁵ Furthermore, given that we lack detailed data about which elements of our intervention were most or least impactful, future evaluations are necessary to assess the impact of individual components of quality improvement strategies such as ours.^{34,35} As our study is among the first to assess a quality improvement strategy targeting HIV status assessment in the context of severe illness triage, continued development of other theory-informed, multi-modal interventions is needed.

This study has several strengths. First, we have provided a large, prospective assessment of HIV-associated severe illness in a rural, high HIV-burden setting. Second, we have identified limited implementation of HIV status assessment as a key challenge to improving hospital-based care in this setting. Third, although the SIMS intervention was not successful at improving HIV status assessment at all sites, the study successes at one site highlight the potential for theory-informed implementation approaches to improve HIV status assessment in a high HIV burden setting.

This study has several limitations. First, we relied on chart documentation of HIV status assessment. Some patients may have had HIV status assessed that was not documented in these records, underestimating the impact of our intervention. Conversely, it is possible that an increased number of febrile illness admissions (diagnosed as malaria) during the study period contributed to increased HIV status assessment at specific sites. Next, as we were unable to distinguish the number of patients assessed

through self-report versus in-hospital PICT, we cannot assess the frequency of acceptance among patients approached for HIV testing or the proportion of new diagnoses. Finally, as we did not assess clinical stage or CD4 cell count, we cannot stratify severe illness frequency or mortality by extent of immunosuppression.

Hospitalized HIV-infected patients in western Uganda are at high risk for severe illness and death. Continued development and evaluation of quality improvement strategies targeting HIV status assessment are needed to enhance hospital-based triage and severe illness management in high-burden HIV settings.

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Contexte : Quatre structures de santé hospitalières dans l'ouest de l'Ouganda.

Objectif : Déterminer l'impact d'un programme innovant multimodal d'amélioration de la qualité sur l'évaluation du statut du virus de l'immunodéficience humaine (VIH) et l'impact du statut VIH sur les états de maladie grave et la mortalité.

Schéma : Une étude échelonnée, pré-post et quasi-expérimentale conçue pour évaluer une intervention multimodale (réunions d'amélioration concertée, audit et rétro-information, tutorat clinique) pour améliorer la qualité des soins après la formation initiale sur la prise en charge de maladies graves dans un contexte de faibles ressources.

Résultats : Entre août 2014 et mai 2015, 5759 patients ont été hospitalisés : 2451 (42,6%) ont eu une évaluation de leur statut VIH et 395 (16,1%) se sont avérés infectés par le VIH. Ces derniers ont été

significativement plus susceptibles de répondre à des critères de choc (27,5% contre 15,1% ; rapport de risque [RR] 1,8 ; intervalle de confiance [IC] 95% 1,7–1,9 ; $P < 0,001$) et de détresse respiratoire grave (6,7% contre 4,3 ; RR 1,5 ; IC95% 1,2–2,0 ; $P < 0,001$), et ont été significativement plus susceptibles de décéder à l'hôpital (12,0% contre 2,9% ; RR 4,1 ; IC95% 3,2–5,4 ; $P < 0,001$). Il n'y a pas eu d'éléments en faveur d'une amélioration de l'évaluation du statut VIH pendant la période d'intervention (36,5% contre 44,8% ; +8,3% ; IC95% –8,3 à 24,8 ; $P = 0,33$).

Conclusions : Les patients infectés par le VIH hospitalisés dans l'ouest de l'Ouganda ont un risque élevé de maladie grave et de décès. De nouvelles stratégies d'amélioration de qualité sont requises afin d'augmenter les tests VIH en hôpital dans les contextes à fardeau élevé de maladie.

Marco de referencia: Cuatro establecimientos hospitalarios en la zona occidental de Uganda.

Objetivo: Determinar la repercusión de un programa innovador multimodal de mejora de la calidad sobre la evaluación de la situación frente al virus de la inmunodeficiencia humana (VIH) y la repercusión del estado frente al VIH en materia de enfermedades graves y mortalidad.

Método: Se realizó un estudio semi-experimental escalonado pre y post con el fin de evaluar una intervención multimodal (reuniones de colaboración para mejorar de la calidad, auditorías y retroalimentación, tutoría clínica) encaminada a mejorar la calidad de la atención, tras una capacitación formal sobre el manejo de las enfermedades graves en entornos con bajos ingresos.

Resultados: De agosto del 2014 a mayo del 2015 se hospitalizaron 5759 pacientes; en 2451 se examinó su situación frente al VIH (42,6%) y 395 presentaban infección por el VIH (16,1%). Los pacientes

afectados por el VIH exhibieron una probabilidad significativamente mayor de cumplir con los criterios diagnósticos de choque (27,5% contra 15,1%; cociente de riesgos [RR] 1,8; intervalo de confianza [IC] del 95% 1,7–1,9; $P < 0,001$) y de insuficiencia respiratoria grave (6,7% contra 4,3%, RR 1,5; IC95% 1,2–2,0; $P < 0,001$) y la probabilidad de morir en el hospital fue significativamente más alta en estos pacientes (12,0% contra 2,9%, RR 4,1; IC95% 3,2–5,4; $P < 0,001$). No se encontraron pruebas en favor de una mejor evaluación de la situación frente al VIH durante el período de la intervención (36,5% contra 44,8%; +8,3%; IC95% –8,3 hasta 24,8; $P = 0,33$).

Conclusión: Los pacientes hospitalizados aquejados de infección por el VIH en Uganda occidental son muy susceptibles de sufrir una enfermedad grave o la muerte. Se precisan nuevas estrategias de mejora de la calidad que refuercen la práctica de las pruebas diagnósticas de infección por el VIH en los entornos con alta carga de morbilidad.