Burden of acute and early HIV infection in an outpatient setting in Shiselweni, Eswatini

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Background

- Unaddressed acute and early HIV infection (AEHI) contributes to continuous HIV transmission
- Diagnosis and care for EAHI is almost non-existent in sub-Saharan Africa and current testing guidelines provide no guidance for AEHI. AEHI diagnosis is challenging due to lack of affordable
- Eswatini has high HIV burden (24.8% HIV prevalence in >15 years old in 2021*). Despite excellent access to HIV care (95-95-95 goals reached in 2021), incidence remains high at 0.62% among >15 years old adults*
- A study** conducted in Shiselweni region in Eswatini in 2019 showed high AEHI burden (3.8%) among patients with symptoms suggestive of AEHI who attended outpatient service. An antigen/antibody rapid diagnostic test (RDT) Alere Combo showed promising performance when used in the laboratory on full blood samples (sensitivity 86.2% and specificity 99.9%).
- To further demonstrate AEHI burden and programmatic feasibility of diagnosing AEHI in routine settings, we incorporated AEHI testing in the routine HIV testing service (including antigen/antibody RDT) within larger study estimating the burden of sexually transmitted infections in 6 clinics in Nhlangano health zone, Shiselweni region

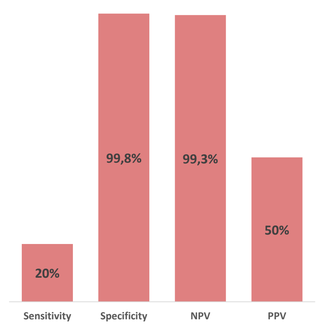
Methods

- Cross-sectional study among adults (>18 years) attending routine HIV testing for whatever reason
- HIV diagnosis:
  - Standard serial rapid tests (RDT, Determine™ and Uni-Gold™ by HIV counselors on finger prick blood
  - In parallel 4th generation antibody/p24 antigen RDT Determine™ HIV Early Detect) by HIV counselors on finger prick blood – for validation purpose only
  - Quantitative RNA detection by Xpert on full blood in the central laboratory
- Definitions:
  - AEHI: negative or discordant RDT and detectable HIV viremia ≥40 copies/mL
  - Chronic HIV infection: positive serial antibody RDT
- Clients newly diagnosed with HIV offered immediate ART initiation and assisted partner notification, & clients testing negative were offered HIV PrEP and PEP prophylaxis
- Performance of Determine™ HIV Early Detect for detection of AEHI was evaluated against quantitative RNA detection as gold standard

Results

- A total of 1122 adults with unknown HIV status were enrolled in the study between July 2022 and March 2023. Median age was 27 years (IQR 22-33) and 690 (61.5%) were women
- Overall, **47 (4.2%) had newly diagnosed HIV infection**:
  - Chronic HIV: 37 (3.3%)
  - **AEHI: 10 (0.9%)** or 10/47 (21.3%) of newly diagnosed HIV cases
- **AEHI characteristics**
  - 2 discordant RDT and 8 negative RDT
  - Clients with AEHI were more likely to be women, younger than 30 years and presented with fever or sore throat.
  - Median viral load: 3.3 M (IQR 0.75M-10.M) copies/ml.
- **Determine™ HIV Early Detect** identified no additional HIV cases compared to Determine™ and overall performance indicators were poor:

Diagnostic group	
True positive	2/10
False positive	2/1066
True negative	1064/1072
False negative	2/4



PPV – negative predictive value; PPV – positive predictive value; ROC – receiver operating characteristic. The 2 false positive and 2 false negative samples were both RDT discordant and also tested positive with routine Determine™ RTD.

Demographic, behaviour and clinical characteristics for enrolled patients, by HIV status

	HIV negative	Chronic HIV	AEHI	P-value
	N = 1075	N = 37	N = 10	
Age <30 years	673 (62.6%)	19 (51.4%)	**9 (90%)**	**0.075**
Female sex	653 (60.7%)	28 (75.7%)	**9 (90%)**	**0.033**
Feeling at risk of HIV	437 (40.9%)	21 (56.7%)	5 (50%)	0.134
>1 sex partners	327 (30.4%)	10 (27.0%)	3 (30%)	0.876
Condomless sex since last HTS	440 (41.3%)	18 (48.6%)	6 (60%)	0.334
Main partner HIV status unknown	428 (39.8%)	21 (56.7%)	6 (60%)	0.205
Last HIV test within last 6 months	830 (77.2%)	**17 (45.9%)**	7 (70%)	**0.001**
PrEP or PEP within last 6 months	129 (12%)	5 (13.5%)	0	0.485
History of fever	205 (19.1%)	11 (29.7%)	**5 (50%)**	**0.006**
History of sore throat	**162 (15.1%)**	**3 (8.1%)**	**3 (30%)**	**0.034**
STI suggestive symptoms	701 (65.2%)	28 (75.7%)	6 (60%)	0.393
AEHI suggestive symptom	755 (72.1%)	31 (84.8%)	8 (80%)	0.255
Diagnosed syndromic STI	426 (39.6%)	11 (29.7%)	6 (60%)	0.197
Lab confirmed STI (NG/CT/TV)	345 (32.1)	15 (40.5)	5 (50%)	0.277

AEHI suggestive symptoms: fever, sore throat or any STI suggestive symptom

- **Linkage to care:**
  - ART initiation: 40/47 clients initiated ART with median delay of 0 days (range 0-63 days); 8/10 clients with AEHI initiated ART
  - PrEP initiation: Among 1075 HIV negative clients, 429 (39,9%) were eligible for PreP after clinical screening; 125 among eligible (29.1%) initiated PrEP

Conclusions & Recommendations

- Overall, AEHI prevalence was 0.9% among patients attending HIV testing and presented 21% of newly diagnosed HIV infections – 1 in 5 HIV cases would have been missed without testing for AEHI
- Prevalence of newly diagnosed HIV was high (4.2%) among patients attending HIV testing services – despite most clients frequently testing for HIV (>70% reported having had last HIV test within past 6 months)
- Clients with AEHI had very high viral load at the time of diagnosis, with high risk of transmitting HIV further. Linkage to care was good, but delay in ART initiation for AEHI cases could be improved if AEHI diagnosis was available at point of care
- Performance of Determine™ HIV Early Detect when used in routine conditions was disappointingly poor; the need for better affordable point-of care diagnostics for AEHI remains urgent.
- Identifying and treating AEHI in routine outpatient settings can contribute to prompt HIV diagnosis and care, thus contributing to epidemic control in generalized HIV epidemic settings.

- *SHIMS 3 2021; **Kerschberger et al, 2022; ***SHIMS 2 2016/7
- Study was approved by Eswatini Human Health Research and Review Board and MSF Ethics Review Board.