Epidemiology of HIV and selected blood-borne infections in East-Africa
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Chapter 12

Summary

East-Africa, after Southern Africa, is the region hardest hit by the HIV pandemic, with severe generalised epidemics seen in every nation. The exact reasons for these high levels of HIV infection are still insufficiently understood. The lack of high quality health information and vital registration systems place a high emphasis on data collected through surveys, surveillance, projections, and modelling to inform policy and programming.

HIV co-infections account for most of the observed HIV-related burden of disease. Many of these co-infections are highly endemic in East-Africa, and account for a substantial proportion of all-cause morbidity and mortality, including TB, malaria, hepatitis viruses, and human herpesvirus 8. Several of these, including hepatitis viruses, malaria, and human herpesvirus 8 have blood transfusion related significance.

Over the last decade, massive international donor assistance facilitated an extraordinary expansion of HIV-related control programmes in East-Africa, resulting in substantial decreases in HIV-related morbidity and mortality, albeit smaller corresponding decreases of new HIV infections or HIV prevalence. In the long-term, these control efforts may transform generalised HIV epidemics into concentrated ones, and demand a shift in HIV surveillance towards HIV incidence and surveys among key populations at increased risk for HIV infection. Successes in malaria control, the shift from commercial and replacement to safer volunteer donors, as well as the expansion of screening and processing procedures of donated blood should make the blood supply ever safer.

In Chapter 1, the research topic areas – HIV surveillance and projections, as well as HIV co-infections and transfusion safety - were introduced and described, along with a description of East-Africa, the setting of all studies presented here.
Part 1 Epidemiology of HIV infection

In Chapter 2, we estimated the burden of HIV disease in Uganda. This work, using HIV survey and programme data collected in Uganda, as well as software to generate demographic and HIV-related estimates, may serve as an example as to how deficits caused by compromised health information systems can be addressed through extrapolation and projection of survey and programme data. It allows for the translation of proportions and rates into absolute burden of disease estimates. One key estimate concerned the total number of people living with HIV/AIDS, which, by 2008, at 1.1 million, we estimated to be as high as it likely was during the peak HIV prevalence year in 1994. Although the adult HIV prevalence, estimated at 6.4% in 2008, was much lower than in 1994, the absolute burden of HIV disease now matched that of the peak years because of the substantial population growth in the intervening years. Although the projection took into account a massive expansion of HIV treatment programmes (from 67,000 in 2005 to 160,000 in 2010), the number of persons with unmet treatment need was estimated to barely decrease from 127,600 to 111,100 in the same years, reflecting again in part population growth as well as the substantial mortality pressure that otherwise removes thousands of lives from the pool of persons with unmet ART needs. Importantly, this work also suggested that the use of single-dose nevirapine averted only a relative small number of paediatric HIV infections, estimated at 4% of all vertical infections occurring in 2005.

Chapter 3 examines the burden of HIV disease in a select key population in Kampala, Uganda, that of men who have sex with men (MSM). The lack of a complete sampling frame for this population required a respondent driven sampling design. Homosexuality is criminalised in Uganda and sampling during this survey was severely hampered by two arrest episodes in Kampala among homosexual activists or alleged homosexual persons during the sampling period. The resulting sample size (N=300) was sufficient to estimate HIV prevalence at 13.8% (95% confidence intervals [CI])
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7.9%-20.1%), approximately three to four times higher than that among general Kampala adult men. In multivariate analysis, HIV infection was found to be positively correlated with a life-time history of homophobic abuse (Odds ratio [OR] 5.4, 95% CI 2.0-14.8). This was the first bio-marker based survey among MSM in Uganda, confirming the indigenous existence of this population and providing important data points and estimates for advocacy and programming.

Chapter 4 examines the utility of routine HIV Prevention of Mother-To-Child Transmission (PMTCT) data in Kenya for the purpose of HIV surveillance. The background to this study are the rapidly expanding PMTCT programmes in East-Africa which provide a plethora of HIV testing data, adding to the ethical concerns of unlinked anonymous HIV testing (UAT) of left-over blood collected from pregnant women without returning the HIV results. The study compared same-clinic 2003 PMTCT and UAT data in Kenya. At that time, the Kenyan PMTCT programme was still in its infancy, and present only in 6/39 clinics. HIV testing for PMTCT too was low at 56%. However, the median UAT-based HIV prevalence was estimated at 12.8%, compared to 14.4% among PMTCT clients at the same clinics. Data quality and accessibility emerged as additional concerns impeding the use of PMTCT data for HIV surveillance.

In Chapter 5, using national survey and HIV programming data in Uganda, we compared the effect of family planning on averting paediatric HIV infections to that by anti-retroviral (ARV) prophylaxis. Comparing several national-level projection scenarios, family planning was found to have averted 19.7% of paediatric infections and 13.1% of paediatric HIV deaths, substantially more than ARV-based interventions in the same year (8.1% and 8.5%, respectively). While ARV-based paediatric HIV prevention programmes are expected to substantially expand quantitatively and qualitatively (through the use of combination ARV regimens) in the ensuing years, the large unmet need for family planning was estimated to have an even larger paediatric HIV prevention potential during the years 2008-12, estimated at 24.5% of infections and...
19.8% of deaths. A surprising, if tangential, finding was that ARV-based PMTCT interventions likely increase the number of orphans by providing a survival benefit for the HIV-exposed offspring compared to their mothers. As infections averted are non-material events, their estimation with modelling and projection software packages likely are the only modes to examine the effect of such interventions.

Chapter 6 describes the effect of HIV disease progression and ART on the specificity of HIV recency assays. We subjected 950 blood specimens collected from 253 known long-term HIV-infected adult in rural Uganda both before and 3, 12, and 24 months after ART initiation. This study reported that the specificity of the BED HIV-1 CEIA assay (with an estimate period of recency of 236 days) decreased with increasing time on ART, from 12.4% pre-ART to 23.8% after 24 months of ART. Interestingly, another HIV recency assay, based on antibody avidity varying by duration of infection, classifies 101 (96.2%) of the 105 false-recent BED results correctly as long-term infections, suggesting that a multi-assay algorithm may increase the overall accuracy of detecting HIV recency.

Part 2 Epidemiology of selected blood-borne infections

Chapters 7, 8, and 9 examine the interface of human herpesvirus 8 (HHV-8) and blood transfusion in Kampala, Uganda. HHV-8 is a classic HIV co-infection, causing Kaposi’s sarcoma and other malignancies, primarily in immunosuppressed individuals.

The high HHV-8 seroprevalence seen in this study provided a rationale to proceed with an observational cohort study among transfusion recipients in Kampala (Chapter 7). This study examined 991 transfusion recipients who were HHV-8 seronegative pre-transfusion and for whom the exact exposure status (transfusion with HHV-8 seropositive or seronegative blood) was known. A total of 41 seroconversions were observed during the scheduled 6 month follow-up. Recipients who received HHV-8 seropositive blood had a 2.8% excess risk (p<0.05) of seroconversion. Most of these excess
seroconversion appeared to occur during 3-10 weeks of follow-up (excess risk 2.7%, p=0.005). Importantly, the study showed that the excess risk is mainly confined to HHV-8 seropositive blood stored for 4 days or less (excess risk 4.2%, p<0.05), consistent with a storage labile infectious agent.

In Chapter 8 the prevalence and risk factors of HHV-8 in candidate blood donors. Of 3,736 specimens, 203 reactive for HIV, Hepatitis B surface antigen (HBsAg), or syphilis were selected, along with 203 specimens non-reactive for any of these three infectious agents. The weighted overall HHV-8 seroprevalence was estimated at 40%. Specimens that were reactive for HIV or HBsAg were more likely to be reactive for HHV-8 as well (p<0.001 and p=0.02, respectively). There was no trend in HHV-8 prevalence by age among these all-adult blood donors, suggesting that the bulk of HHV-8 transmissions may have occurred prior to onset of adulthood.

The last part of the HHV-8 and blood safety related research concerned the risk of death among transfusion recipients in the same cohort study (Chapter 9). This study examined 1,092 recipients that were HHV-8 seronegative pre-transfusion, survived at least 7 days, and, through linked blood donor data, were known to have been transfused either exclusively with HHV-8 seronegative blood or had received at least one HHV-8 seropositive blood product. A total of 111 deaths occurred during follow-up. After controlling for known confounders, recipients who received HHV-8 seropositive blood that was stored for only 4 days or less were more likely to die than unexposed recipients (adjusted HR [AHR] 1.92, 95% CI 1.21-3.05). The increased hazard of death was also seen when limiting the analysis to recipients of a single transfusion (AHR 1.95, 95% CI 1.10-3.45). Moreover a dose response effect was observed, as each additional HHV-8 seropositive transfusion increased the hazards of death further (AHR 1.79, 95% CI 1.33-2.41). The exact mechanism through which HHV-8 might cause death via transfusion is not known, and the possibility of unknown confounders cannot be ruled out.
Chapter 10 examines the prevalence of hepatitis C virus (HCV) in candidate blood donors in Kampala, Uganda. At the time of this study, donated blood was not yet screened for HCV. Of 2,592 specimens tested, 107 (4.1%) were HCV Enzyme Immuno Assay (EIA) reactive and 15 (0.6%, 95% CI 0.3%-0.9%) were Recombinant Immuno Blot Assay (RIBA) reactive. Already implemented routine screening for HIV, HBsAg, and syphilis would only remove approximately 20% of potential HCV-positive blood units. The screening costs for per potential transfusion-associated HCV infection (i.e., exposure to RIBA-positive blood) averted were estimated at $782, a considerable cost factor for Uganda’s low income setting.

A prospective cohort study of blood transfusion recipients in Kampala, Uganda examined the effect of HIV infection on morbidity and mortality in paediatric (under 5 years of age) transfusion recipients with malaria (Chapter 11). Among 847 children examined, 9.2% were HIV-infected. After controlling for confounders, HIV-infected transfusion recipients were shown to experience a higher risk of death within 7 days (hazards ratio [HR] 2.86, 95% CI 1.30-2.69) and within 28 days (HR 3.70, 95% CI 1.91-7.17) than HIV-uninfected transfusion recipients. This risk further increased by the end of the 6 month follow-up time (HR 5.70, 95% CI 3.54-9.16). All study participants were ART-naive. These findings suggest that children transfused for malaria warrant HIV testing upon admission and aggressive treatment if found HIV-infected.

In Chapter 12, the study findings are re-evaluated and their significance and implications for additional research is discussed.