ABSTRACTS

‘Excelling in Clinical Care’: Southern African HIV Clinicians Society Conference

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The top nine best abstracts from the biennial Southern African HIV Clinicians Society Conference, held in September 2014, are provided here. Presentations from the conference may be viewed online: http://sahivsoc2014.co.za/2014-speaker-presentations/


First place

This abstract includes the updated data presented by Dr Govender at the conference; these data are not included in the printed conference programme.

Cryptococcal screen-and-treat in Gauteng Province, South Africa: Update from the first 2 years of implementation, 2012 - 2014

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Category: Non-tuberculosis Opportunistic Infections

Background. Screening for early cryptococcal disease is recommended to reduce morbidity/mortality related to HIV-associated cryptococcal meningitis (CM). Our objective was to describe the cascade of care among patients with a positive plasma cryptococcal antigen (CrAg) test. Our goal was to determine whether screening patients had prior CM. Incident antigenaemia (IA) was defined as a patient with a positive plasma CrAg test and no prior CM.

Methods. Screening started in September 2012 at 21 facilities in Johannesburg, and in April 2013 at 87 Ekurhuleni facilities. Remnant plasma from any routinely collected ethylenediaminetra-acetic acid (EDTA) sample with a CD4+ count <100 cells/µL was tested with CrAg lateral flow assay (ImmunoMycologics, USA). At 45 enhanced surveillance (ES) facilities, surveillance officers reviewed medical records of plasma CrAg-positive patients from September 2012 to August 2014. Cases of incident CM were reported to national surveillance. CrAg screening and CM surveillance data were cross-matched to determine whether screened patients had prior CM. Incident antigenaemia (IA) was defined as a patient with a positive plasma CrAg test and no prior CM.

Results. During the evaluation, 18 357 patients were screened, 820 (4%) of whom were plasma CrAg-positive. Of 624 diagnosed at an enhanced surveillance facility, 457 (73%) had data available for CM and IA diagnosis. Of these, 207 (45%) had prior CM. Of 250 (53%) with IA, symptom data were available for 244. Of these, 99 (41%) had headache and/or confusion, and 145 (59%) were asymptomatic. Lumbar puncture (LP) was performed for 56 (57%) and 48 (32%) of symptomatic and asymptomatic patients, respectively. Excluding those with confirmed CM, available data showed that almost all patients with IA (symptomatic: 41/42 and asymptomatic: 98/99) were prescribed fluconazole. Of 48 ART-naive patients with IA and known ART status, 47 initiated ART a median of 15 days (interquartile range 13 - 29) post screening.

Conclusions. Approximately 40 patients with CD4+ count <100 cells/µL needed to be screened to detect an IA case. Most with IA were initiated on antifungal treatment and ART.

Outcomes in HIV-infected and -uninfected drug-resistant tuberculosis patients in Khayelitsha, South Africa

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Category: Tuberculosis

Background. There are limited data on outcomes of HIV-infected, drug-resistant tuberculosis (DR-TB) patients who are on antiretroviral therapy (ART). We compared outcomes among HIV-infected and -uninfected patients treated for DR-TB in Khayelitsha, South Africa.

Methods. Routine data of patients diagnosed with DR-TB in Khayelitsha from January 2008 to December 2011 were analysed retrospectively. Outcomes until December 2013 were included.

Results. A total of 875 patients were diagnosed with DR-TB. Overall, 607 (69%) were HIV-positive, 232 (27%) HIV-negative, with status unknown in 36 (4%). Among HIV-positive patients, 96 (16%) had pre- and extensively drug-resistant TB (XDR-TB), 373 (61%) had multidrug-
resistant TB (MDR-TB), 129 (21%) had rifampicin monoresistance, and 9 (1%) had presumed DR-TB. Among the HIV-positive patients, 34 (15%) had pre- and XDR-TB, 144 (62%) had MDR-TB, 28 (12%) had rifampicin monoresistance and 26 (11%) had presumed DR-TB. A total of 139 (16%) patients did not start DR-TB treatment; 64/139 (46%) died before treatment initiation (55 HIV-positive, 7 HIV-negative; p<0.001). Among those who started DR-TB treatment, 507/736 (69%) were HIV-positive. Of these 507 patients, 470 (93%) were on ART, with 236 (47%) already on ART at DR-TB diagnosis; median CD4+ count was 120 cells/mm³ (interquartile range 55 - 250). Among those with final outcomes (642), treatment was successful in 213/440 (48%) and 88/189 (47%) of HIV-positive and HIV-negative patients, respectively. More HIV-negative patients were lost from treatment (LFT) (37% HIV-negative vs. 27% HIV-positive, p=0.01). Mortality was greater among HIV-positive patients (18% HIV-positive vs. 9% HIV-negative, p=0.004) during treatment. There was no difference in treatment failure: 26/440 (6%) HIV-positive and 14/189 (7%) HIV-negative patients failed treatment (p>0.05). Patients who subsequently died included 31/120 HIV-positive and 15/70 HIV-negative patients who were LFT, and 21/26 HIV-positive and 7/14 HIV-negative patients with treatment failure. There was no significant difference in overall mortality: 19/100 person-years (95% confidence interval (CI) 16 - 22) HIV-positive; 17/100 person-years (95% CI 12 - 22) HIV-negative; incidence rate ratio 1.14 (95% CI 0.80 - 1.67).

Conclusions. In the presence of ART, treatment success, treatment failure and long-term mortality were similar in HIV-positive and HIV-negative DR-TB patients. HIV-positive patients on ART experienced greater mortality prior to and during DR-TB treatment. LFT masked mortality in both HIV-positive and HIV-negative patients, with more LFT among HIV-negative patients and 20% mortality thereafter. More effective treatment regimens and strategies for reducing LFT are needed to reduce mortality in DR-TB patients.

A case series of antiretroviral therapy-associated gynaecomastia

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Category: Antiretroviral Treatment

Background. Gynaecomastia is associated with antiretroviral therapy (ART). There are few data about the clinical characteristics of patients with ART-associated gynaecomastia and optimal management of this adverse drug reaction (ADR). The National HIV and TB hotline at the Medicines Information Centre offers the following standard advice for ART-associated gynaecomastia: measure free testosterone to exclude hypoandrogenism and substitute efavirenz.

Objective. To describe the clinical characteristics, management and clinical outcomes of reported gynaecomastia cases.

Methods. We identified all cases of gynaecomastia in HIV-infected patients on ART reported to the hotline between June 2013 and Jan 2014. We collected data on actions taken and clinical outcomes.

Results. Twenty-nine suspected gynaecomastia cases were reported, representing 11% (29/274) of total ADR queries received during this period. All were on efavirenz-based regimens, and median age was 33 years (interquartile range (IQR) 17- 40). The median onset of gynaecomastia post efavirenz initiation was 19 months (range 2 - 99). Twelve patients (41%) had bilateral gynaecomastia, 8 (28%) had unilateral gynaecomastia and 9 (31%) were unknown. Five (17%) patients were on additional drugs associated with gynaecomastia: 1 on amiodipine and 4 on isoniazid. We obtained follow-up information on 21 (72%) patients, with a median follow-up of 62 days (IQR 39 - 97). Free serum testosterone was performed in 13 of 21 patients; 11 had normal testosterone and 2 were unknown. Of patients with follow-up, 18 substituted efavirenz, of whom 4 (22%) improved, 1 (5%) deteriorated, 5 (28%) remained unchanged and 8 (44%) had unknown status. Among patients continuing efavirenz (n=3), 2 were unchanged and 1 had unknown status.

Conclusion. Efavirenz-associated gynaecomastia was frequently reported to the hotline. Improvement of gynaecomastia after substitution was variable, and since efavirenz is a component of the preferred first-line ART regimen, more evidence to guide optimal management of this ADR is needed. Usefulness of free testosterone level testing requires further study.

Determinants of resistance to second-line protease inhibitor-based antiretroviral therapy in the southern African private sector

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Category: Antiretroviral Treatment

Background. In the South African public sector, 11% of patients failing second-line protease inhibitor (PI)-based antiretroviral therapy (ART) have PI resistance. We explored predictors of PI resistance in patients on second-line ART in a private sector cohort from 2004 to 2013.

Methods. We categorised patients as having PI resistance if their genotype included ≥1 major resistance mutations to their current PI. We constructed a multivariate logistic regression model, including age, sex, PI duration, adherence by pharmacy claims for 4 months prior to resistance test, and viral load (VL) closest to resistance test.

Results. There were 339 patients with at least 4 months of second-line PI-based ART. Mean age was 42 (standard deviation 8) years, 211 (62%) were female, and 309 (91%) were on lopinavir and 30 (9%) on atazanavir. There were ≥1 major PI-resistance mutations in 147/339 (43%). Median duration on PI-based ART before genotype was 2.5 years (interquartile range (IQR) 1.4 - 4.4). Median VL before genotyping was 85 586 copies/mL (IQR 18 893 - 242 103). Having a major PI-resistance mutation was independently associated with age (odds ratio (OR) for 10-year age increase 2.0, 95% CI 1.4 - 2.8), highest quartile of ART duration (OR 2.7, 95% CI 1.4 - 5.3), and with the highest three adherence quartiles (OR 2.1, 95% CI 1.0 - 4.3; OR 2.4, 95% CI 1.1 - 4.9; OR 2.6, 95% CI 1.3 - 5.2 for 66 - 93%, 94 - 98% and 99 - 100% adherence, respectively). Sex and VL at the time of resistance testing were not associated with PI resistance.

Conclusion. In this private sector cohort, the proportion with PI resistance was higher than in public sector studies, which may reflect a longer duration of second-line ART. These results suggest that patients with longer duration of PI-based ART or adherence >65% may be most likely to benefit from genotyping.
Gender differences and the effect of pregnancy on antiretroviral treatment outcomes amongst adolescents in South Africa

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Category: Children and Adolescents

Abstract

Background. Adolescence is an important age group for HIV care and treatment programmes, as adolescents have a high rate of HIV acquisition, and perinatally infected children are transitioning into adolescence. Relatively little data comparing gender differences in adolescent ART outcomes in low-income settings are available.

Objectives. To investigate gender differences in baseline characteristics and antiretroviral therapy (ART) outcomes in a large multicentre cohort in South Africa (SA).

Methods. Routine clinical data from 82 public ART facilities in four provinces in SA were analysed. ART-naive adolescents (ages 9 - 19 years) starting ART between 2004 and 2011 were included. The outcomes were: mortality, loss to follow-up (LTFU), viral suppression (<400 copies/mL) and virological failure (two consecutive viral loads >1 000 copies/mL) after starting ART. Competing risks regression and generalised estimating equations were used to analyse outcomes controlling for individual and site-level confounding.

Results. A total of 3 175 adolescents were included, of whom 2 123 (66.9%) were adolescent girls. Pregnancy among girls who started ART increased progressively over time, and reached 25.3% by 2011. The median baseline CD4+ cell count of pregnant girls was substantially higher than for non-pregnant girls (205 v. 143 cells/µL; p=0.0001). LTFU was substantially higher in pregnant girls, adjusted subhazard ratio=1.94 (95% confidence interval (CI) 1.03 - 3.65; p<0.040). Viral suppression on ART was lower in pregnant girls, adjusted odds ratio=0.58 (95% CI 0.39 - 0.86; p=0.006). Confirmed virological failure was substantially increased among pregnant girls, adjusted hazard ratio=4.85 (95% CI 1.78 - 13.1; p=0.002).

Conclusion. There were high levels of pregnancy among adolescent girls who started ART, and they had less-advanced HIV disease, likely owing to earlier diagnosis at maternal facilities. However, pregnant girls had increased LTFU and poorer virological outcomes. Programmes to reduce adolescent pregnancy and increased ART adherence support for pregnant adolescents may be important interventions to improve outcomes of adolescents and to reduce vertical HIV transmission.

HIV is the primary exclusion criterion in a PrePex male circumcision device introductory study in Mozambique

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Category: Prevention

Abstract

Background. Voluntary medical male circumcision (VMMC) reduces female to male HIV transmission by ~60%, and is recommended by the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) as a priority intervention in high-HIV prevalence settings. In Mozambique, VMMC for HIV prevention started in November 2009; >300 000 males were surgically circumcised by March 2014, with a goal of 2 million by 2016. PrePex could potentially reduce procedure time and increase acceptability of VMMC because it does not require injectable anaesthesia or suturing. In 2013, an introductory study of the PrePex device was conducted in Maputo, Mozambique, to assess acceptability among providers and clients.

Methods. Adult clients presenting for VMMC at the study site in Maputo were offered surgical or PrePex device circumcision. Those who preferred PrePex were screened for inclusion criteria. Exclusion criteria were recorded. The current guidelines excluding infected men from device circumcision are from the WHO.

Results. During the study, 752 clients aged ≥18 years were presented for VMMC, and were offered the choice of PrePex or conventional surgery; 116 (15.4%) preferred surgical VMMC. Of the 636 clients who chose PrePex, 132 (20.8%) were ineligible. HIV infection was the primary reason for exclusion, restricting 85 (64%) interested seropositive clients. Phimosis or narrow foreskin was present in 17 (13%) of the ineligible clients. Sixteen clients (12%) were unable to communicate in Portuguese and 8 (6%) lacked communication means (cellphone), which were study requirements. The remaining 6 (5%) were excluded due to an active sexually transmitted infection, sexual dysfunction or previous penile surgery.

Conclusions. One-third of adult clients offered PrePex either did not want device circumcision or were ineligible under current guidelines, which exclude HIV-positive men. An integrated programme offering both device and surgical VMMC remains the best service delivery option. However, there is a need to assess the safety of PrePex among HIV-positive clients, as HIV testing in Mozambique is recommended but not required in routine VMMC service delivery.

Analysis of the antiretroviral treatment clinical outcomes in South Africa from 2004 to 2012

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Category: Antiretroviral Therapy

Abstract

Objectives. To analyse loss to follow-up (LTFU), retention on antiretroviral treatment (ART), viral load (VL) suppression and increase in CD4 counts on adult patients in the South African public sector national ART programme.

Methods. This was a cohort study including all patients who started ART in the South African public sector facilities from 2004 to 2013. ART data were collected routinely through the National TIER.Net database and exported to the District Health Information System (DHIS) in the form of excel pivot table workbooks. National analysis of data by financial years was conducted to determine improvements in retention on ART, CD4 counts, VL suppression and LTFU.

Results. Data summarised patient clinical outcomes for 435 323 adult patients who started receiving ART from April 2004 to June 2013. Adult patients starting ART increased exponentially from 2 189 in 2004/5 to 119 827 in 2012/13. The proportion of patients with a CD4+ count of between 200 - 350 cells/µL increased from 8.9% in 2004/5 to 46.7% in 2012/13, while the proportion of patients with a CD4+ count <100 cells/µL decreased from 23.4% in 2004/5 to 4.5% in 2012/13.
Outcomes of infants starting antiretroviral therapy in southern Africa, 2004 - 2012


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Category: Children and Adolescents

Background. There are limited published data on the outcomes of infants starting antiretroviral therapy (ART) in routine care in southern Africa. We described baseline characteristics and outcomes of infants initiating ART at 11 sites contributing to the International Epidemiology Database to Evaluate AIDS in Southern African (IeDEA-SA).

Methods. ART-naive, HIV-infected infants <12 months of age at initiation of ≥3 antiretroviral drugs after 2003 were included. Kaplan-Meier estimates were calculated and Cox Proportional Hazards models stratified by site were used to determine baseline characteristics associated with outcomes mortality and virological suppression. Loss to follow-up (LTFU) was defined as no visit for >9 months prior to site database closure.

Results. The median age of 4 945 infants who initiated ART was 5.9 months (interquartile range (IQR) 3.7 - 8.7). Median follow-up time was 11.2 months (IQR 2.8 - 20.0). At ART initiation, 75% of infants had World Health Organization (WHO) clinical stage 3 or 4 disease, and 85% met the 2006 WHO definition of severe immunosuppression. Three-year mortality probability was >15% and LTFU 29%. Severe immune suppression (adjusted hazard ratio (aHR) 2.19, 95% confidence interval (CI) 1.44 - 3.35), WHO stage 3/4 (aHR 1.36, 95% CI 1.04 - 1.78), anaemia and lower weight-for-age z-score were associated with higher mortality. Initiation of treatment after 2009 was associated with lower mortality (aHR 0.75, 95% CI 0.59 - 0.94). The probability of virological suppression at 6 months and 12 months was 28% and 56%, respectively. Initiation of treatment after 2009 was the only predictor of virological suppression.

Conclusion. The proportion of infants initiating ART with baseline disease severity and high probability of mortality and especially LTFU is a concern. However, the majority of those remaining in care had good virological responses on ART.