MSF@ICASA2017

ABSTRACTS

Effect of routine viral load monitoring on the speed to detect antiretroviral treatment failure in Guinea

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Background

The World Health Organisation has recommended viral load (VL) testing to diagnose and confirm antiretroviral treatment (ART) failure. However, access to routine viral load testing remains limited in resource-constraint settings. Médecins Sans Frontières (MSF) is supporting the phasing out of targeted viral load monitoring (TVLM) in favour of routine viral load monitoring (RVLM) in Guinea.

Objectives

We aimed to evaluate the contribution of RVLM to early diagnosis of treatment failure.

Methods

We conducted a longitudinal study of patients receiving first line ART in nine health facilities supported by MSF in Conakry between 2003 and 2016. A RVLM was defined as a VL measurement between 6 and 12 months of ART initiation. A TVLM was considered as a VL to confirm suspected treatment failure based on clinical and immunological criteria or a catch up VL targeted to a patient on long-term ART without a previous VL. The threshold for defining virological failure was 1000 copies/ml. We used a multilevel survival analysis based on mixed-effects Weibull regression with random effects for health facilities and year of ART initiation, to model the effect of RVLM and covariates on the time to detect virologic failure.

Results

Of 7360 adult patients with a median age of 39 years (IQR: 32 – 47) 5273 (72%) were women. RVLM was done in 889 (12%) patients while 6471 (88%) patients had a TVLM. Virologic failure was detected in 681 (9%) patients at an incidence rate of 20.9/ 1000 person-years (PY) (95%CI: 19.4 – 22.5). The approach-specific detection rates were 77.3/1000 PY (95%CI: 60.4 – 99.0) and 19.4/ per 1000 PY (95%CI: 18.0 – 21.0) in the RVLM and TVLM group respectively (p<0.0001). The time to detect a 25th percentile of failures was drastically reduced from 9.0 years (95%CI: 8.7 – 9.9) during TVLM to 1.9 years (95%CI: 1.7 – 1.9) during RVLM. After adjusting for covariates, treatment failure was detected earlier in patients with active tuberculosis (aHR = 1.87, 95%CI: 1.13 – 3.11) but less frequently in women previously enrolled in PMTCT programmes (aHR = 0.53, 95%CI: 0.36 – 0.79) and in stable patients on a six-monthly appointment for clinical visits (aHR = 0.07, 95%CI: 0.06 – 0.10).

Conclusion

The Joint United Nations Programme on HIV/AIDS target for VL suppression of 90% has been achieved in this Guinean ART cohort. The on-going scaling up process of RVLM has attained 'cruising speed' to detect virologic failure and should be sustained.

Outcomes of HIV-infected persons receiving treatment for Kaposi sarcoma in Conakry, Guinea

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Background

Médecins Sans Frontières is supporting comprehensive HIV care and treatment for Kaposi Sarcoma (KS) including chemotherapy in Guinea, where antiretroviral coverage is low and access to KS treatment is very limited.

Objectives

We aimed to evaluate treatment response and survival outcomes among HIV-infected patients with KS in this setting.

Methods: Retrospective analysis of routinely collected clinical data of HIV-infected patients with KS, receiving ART and chemotherapy consisting of a combination of bleomycin and vincristine at the Donka National Hospital in Conakry between 2012 and 2015.

Results

A total of 225 patients were enrolled for KS treatment, of whom 145 (64.4%) females. Late presentation with stage T1 disease was common (82.7%). At the end of a median of 8 cycles of chemotherapy (IQR: 2 – 12), complete remission was observed in 65 (28.9%), partial remission in 53 (23.6%), stable disease in 15 (6.7%) and unknown response for all 92 (40.9%) patients who lost to follow up (LTFU). The odds of achieving complete remission doubled after every cycle of chemotherapy (aOR = 2.09 95%CI: 1.44 – 3.01) but were reduced by about two-thirds for every month delay between treatment and onset of KS (aOR = 0.31, 95%CI: 0.11 – 0.86). Treatment response was seriously compromised in patients with woody skin oedema (aOR = 0.05, 95%CI: 0.01 – 0.38) and those with prior chemotherapy (aOR = 0.21, 95%CI: 0.05 – 0.80). The median survival time was 7.6 months (95%CI: 5.9 – 9.8). Mortality and LTFU from care were reduced by 22% for every cycle of chemotherapy administered (aHR = 0.78, 95% CI: 0.71 – 0.84) and they were about 20 times lower in those with complete remission compared with those with partial or no response (aHR = 0.05, 95%CI: 0.007 – 0.43).

Conclusions & Recommendations

The overall response rate is 52.4%. Poor outcomes were not uncommon and were largely due to late presentation and LTFU on treatment. Efforts towards early HIV/KS diagnosis and support patient to remain on treatment to a full round of chemotherapy are needed for optimising outcomes. Newer drugs such as pegylated liposomal doxorubicin are required to improve response rate.

Keywords

HIV, Kaposi sarcoma, antiretroviral therapy, chemotherapy, Guinea

Clinical and Immunological HIV Outcomes in a Conflict Setting in the Central African Republic: A Retrospective Analysis

Background

The Central Africa Republic, a chronic medical emergency even before inter-communal violence, displacement, and political instability re-erupted in 2013, has the highest mortality rate for people living with HIV (PLWHA) in the world, with 7,800 deaths in 2015 alone in the small country of only 4.5 million people. The 120,000 PLWHA living in CAR face persistent anti-retroviral therapy (ART) stock-outs and low quality of care in the few facilities in the country that treat HIV (only 25% of PLWHA are estimated to be on ART). Many PLWHA must also must contend with daily instability due to the enduring crisis.

Methods

Medecins Sans Frontieres has been treating HIV in Carnot, in the southwest of the country, since 2011, and in Paoua in the northwest, since 2013. We conducted a retrospective analysis of routinely collected medical data to assess clinical, demographic, and treatment characteristics of HIV-infected adult and pediatric patients under HIV care from January 2011 to July 2017 in Carnot and October 2013 to July 2017 in Paoua. Descriptive statistics were used to analyze outcomes and WHO standard definitions were used throughout.

Results

At the two MSF sites, 4995 HIV-infected individuals were enrolled in care in Carnot and Paoua, respectively, and 4123 (82.5%) initiated treatment. 1733 (34.7%) of enrolled patients were lost to follow up (LTFU) (or were displaced), and another 543 (10.8%) died while under care. 3188 (63.8%) of patients received a baseline CD4 test, revealing that 929 (29.1%) of those tested presented to HIV care extremely immunosuppressed (CD4 <200 cells/μL). Of those who initiated ART, 116 (2.8%) received a 2nd line treatment regimen. CD4 recovery for all patients was 121 cells/μL (IQR 2.0-226.0) after 12 months.

Conclusions & Recommendations

Despite an extremely challenging, conflict affected environment, HIV care provision and continuity was feasible by using context adapted approaches. Displacement due to conflict lead to high levels of LTFU, though many were able to transfer to new facilities to continue ART. Chronic instability and weak health systems should not prevent actors from responding to the needs of populations that lack access to HIV services, especially in places with extremely high HIV mortality like CAR. Contingency planning and program flexibility are critical to success.

Implementing a point of care diagnostic technology package to improve diagnosis and management of patients with advanced HIV in a high prevalence setting; lessons from rural Kenya

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Author Keywords

Point of care testing, advanced HIV, sub-saharan Africa

Background

Two thirds of the HIV positive patients admitted at the Homabay medical in-patient wards (IPD) present with advanced HIV. Rapid accurate diagnosis of some opportunistic infections using point of care diagnostic technology (POC-DT) allows prompt initiation of correct treatment. From April 2015, we implemented a POC-DT package in the IPD. We present an analysis of data from the period March to June 2017.

Objectives

The objective of the MSF-MoH IPD intervention is to improve quality of care and reduce the morbidity mortality of patients in Homabay IPD with emphasis on HIV positive patients.

Methods

Nine different POC-DTs were put in place, with 3 core tests (Alere PIMA™ CD4; IMMY CrAg® LFA, Cryptococcal Antigen Lateral Flow Assay; Alere Determine™ TB LAM Ag); and 6 none-core tests (Hemoglobin, Malaria, Creatinine, Glucose, HepB and Urinalysis). IPD staff were trained on conducting tests and interpreting results. Preventive equipment servicing and quality assurance systems were set up. POC-DT results were documented in patient files and POC-DT registers. Data were collected as part of periodic evaluation. Chi-square test used to explore gender differences, workflow analysis was conducted to document potential time gains.

Results

A total of 357 patients were admitted in the IPD during the period; 55.5% female. Among these, 64.2%(229) were HIV positive with no gender differences (males 63.5% vs females 64.7%, p=0.25). Of those HIV positive, 76.4% (175/229) had a POC CD4 test done at admission. Median CD4 was 194[IQR 77 -421] with 30.9% being less than 100 cells/mm; (males 38.2% vs females 26.2% p=0.09). Of those with CD4 less than 100, 74.1% (40/54) received a reflex serum CrAg test with a positivity of 25%. A total of 78 TB LAM tests were done with a positivity of 53.9% (42/78) and no gender differences (males 46% vs females 70%, p=0.18). A total of 2,448 non-core POC tests were carried out in the same period; 96 Hepatitis B, 768 Glucose, 661 Creatinine, 559 Hemoglobin and 368 Malaria tests. Workflow analysis revealed significant potential time gains comparing POC-DT and standard of care; 75% to 83% on the core tests and 67% to 80% on none-core tests.

Conclusions and Recommendations

Implementation of POC-DTs as a package of routine tests a low resource setting is feasible and resulted in good coverage of CD4 at admission and reflex cryptococcal testing among those with very low CD4. Significantly high cryptococcal and TB LAM positivity were noted.

Characteristics Associated with HIV Viral Suppression: Results from a Retrospective File Review of an HIV Cohort in Rural Kenya

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Background

As we make progress towards the UNAIDS 90-90-90 targets, it is important to understand the factors associated with HIV viral suppression and non-suppression among patients who are on anti-retroviral therapy. We explored factors associated with viral suppression on ART from a retrospective file review conducted as part of routine program evaluation in western Kenya.

Objectives

The joint Ministry of Health (MoH)-Medecins Sans Frontieres(MSF) program aims to improve quality of HIV care in 33 decentralized MoH facilities in Ndhiwa sub-county Kenya. The objective of the evaluation was to develop robust estimates of viral suppression in these facilities and assess the characteristics associated with viral non-suppression to inform programming.

Methods

Through multistage cluster random sampling 4,890 patient files were selected from 17 facilities for retrospective file review. Multivariate logistic regression models were used to explore the association between VL< 1,000 cp/mL and key variables of interest: including sex, age, time to ART, duration on ART, history of ART change and current retention on care status.

Results

Older individuals were more likely to be suppressed with odds between 2.6 and 7.4 depending on age group: (OR[95%CIs] 2.63[1.26-5.45], 6.88[3.45-13.72], 5.18[3.76-7.11], 7.48[4.16-13.4] respectively for 15 to 19 yrs, 20 to 24 yrs, 25 to 59 yrs and ≥ 60 yrs; compared to 0 to 9 yrs). Other variables associated with better odds of suppression include; an interval of >36 months between diagnosis and ART initiation, OR 1.68[95%CI, 1.04-2.71]; ART treatment duration of > 36 months OR 1.61[95%CI, 1.01-2.57], being 'alive and on ART' OR 2.7 [95%CI, 1.06-6.69] and having no history of ART change OR 2.79 [95%CI 2.12-3.66].

Conclusions and Recommendations

Age and history of ART change were strongly associated with VL suppression on ART. To achieve the last 90 of the UNAIDS targets efforts need to be place on pediatric and adolescent care and retaining individuals on care.

HIV Drug resistance asHIV Drug resistance associated with second line antiretroviral regimens failure and virological outcomes of third line regimens in Arua Regional Referral Hospital, Uganda

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Background

The number of patients on 2nd line antiretroviral therapy is growing, but data on HIV drug resistance patterns associated to 2nd line failure in resource constrained settings are scarce. Access to drug resistance test (DRT) is an issue in many countries.

Objectives

We aimed to i) describe HIV drug resistance patterns, ii) investigate the factors associated with extensive resistance to nucleoside reverse transcriptase inhibitors (NRTI), iii) describe the virological outcomes of 3rd line regimens, in patients failing 2nd line in HIV clinic supported by Médecins Sans Frontières at Arua Regional Hospital, Uganda.

Methods

We included all patients followed in Arua HIV clinic who failed on 2nd line (defined with two consecutive viral load (VL) ≥1000 copies/ml by semi-quantitative "SAMBA 1 point-of-care test") and who had a DRT performed at the Uganda Virus Research Institute, Entebbe, from September 2014 to March 2017 to a retrospective analysis. Logistic regression was used to investigate factors associated with extensive resistance to NRTI (NRTI genotypic sensitivity score "GSS"≤1).

Results

78 patients were included: 42% females, median age 31 years [IQR 15-45] and median time of 29 months on 2nd line. Among 70 cases with DRT results (8 failed amplification), most frequent subtypes were A (47%) and D (40%); 18,5% had ≥1 major protease inhibitor (PI) mutation (most frequent: M46I/L, V82A); 82,8% had ≥1 NRTI mutation (most frequent M184V) and 38,5% had NRTI GSS ≤1; 12% had wild type virus. A nadir CD4 count ≤100/mm^3 was associated with NRTI GSS ≤1 (OR 3,9, 95%CI [1,2-14,6], adjusted on age and time on 2nd line). 42,8% of patients who had DRT results were switched to 3rd line, as a minimum composed of integrase inhibitor and PI (40% atazanavir/r, 60% darunavir/r). Median time between 2nd line failure and treatment adaptation was 11,9 months [IQR 8,3-17,5]. At the time of analysis, among 30 patients switched to 3rd line, 8 had VL available at month 6 and 6 at month 12: 5 (62,5%) and 5 (83,3%) were <1000/ml respectively.

Conclusion

Our study highlights the need for access to DRT, in order to avoid unnecessary switch to 3rd line, and access to 3rd line drugs for adults and children (particularly integrase inhibitor) for the management of 2nd line failure. Low nadir CD4 count was associated with extensive resistance to NRTI and might be an indicator of 3rd line requirement in case of second line failure.

Preliminary results of evaluation of the use of GeneXpert HIV-1 Qual assay for decentralized Early Infant Diagnosis

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Background

Delays in EID results among HIV exposed infants result in high morbidity and mortality. In Malawi, EID is conventionally performed in central laboratories using Abbott RealTime HIV-1 Qualitative assay resulting in delayed diagnosis and ART initiation. As part of larger feasibility study, we assessed diagnostic accuracy and outcomes of implementing Cepheid GeneXpert HIV-1 assay (GeneXpert) for EID in decentralized settings in southern Malawi.

Methods

The study was conducted at six facilities in Nsanje District. Enhanced identification of infants, from birth to 18 months, was implemented in three facilities and participant's dried blood spots samples were tested with GeneXpert in parallel with Abbott, a reference test. Conventional EID Abbott only testing was implemented in other three facilities. These results are based on participant's samples taken between May 2016 and May 2017.

Results

506 exposed infants, median age 6 weeks (IQR: 0-8), were identified using enhanced approach and had paired tests results; 43.87% were VEID (infants <6 weeks) and 56.13% were EID (6 weeks-18months). 6/222 (2.7%) VEID and 9/284 (3.17%) EID were positive on paired test. 194 exposed infants from conventional sites had Abbott result available, 14 (7.22%) were positive. 23.53% (96/408) of mothers with exposed infants had high VL result (>1000copies/ml). 6.25% (6/96) of HIV-positive infants, their mothers had high VL result and 1.92% (6/312) of HIV-positive infants; their mothers had suppressed VL (*p-value 0.038*).

The sensitivity and specificity of GeneXpert was 100% (95%CI; 78.2 - 100%) and 99.8% (95%CI; 98.9 - 100%) respectively. GeneXpert showed 100% NPV assuming HIV prevalence of 12.1% in Nsanje District and PPV of 93.8% if 3% of infants were HIV positive, increasing to 99.8% at 4.84% HIV prevalence.

TAT from sample collection to availability of results at a facility was 5 days (IQR: 3 - 9) for GeneXpert; 70 days (IQR: 55-88) and 71 days (IQR: 52 – 93.5) for Abbott at enhanced and conventional sites respectively. 13/15 infants (5/15 VEID) at enhanced, and 8/14 infants at conventional sites were initiated on ART. Median time from availability of Abbott results at health facility to ART initiation 37.5 days (IQR: 25 – 93) and 3.5 days excluding infants with PSHD at enhanced sites and conventional sites respectively. 2/15 and 1/14 HIV-positive infants from enhanced and conversional sites died before Abbott results were ready respectively.

Conclusion

The study results indicate that GeneXpert is a promising test for decentralised EID testing. Considerably short TAT for GeneXpert would potentially reduce delays in ART initiation among infants.

Keywords: HIV-1 Early Infant Diagnosis, Dried blood spot, low-resource settings

Audit of the management of patients with advanced HIV infection hospitalized at Kinshasa Kabinda Hospital Centre (KHC), DR Congo

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Background and Rationale

HIV-related mortality remains high in Africa, particularly in West and Central Africa. The Kabinda Hospital Center in Kinshasa is a 41-bed hospital specializing in the care of HIV patients managed by Médecins Sans Frontières. Intra-hospital mortality was 28% in 2016, with an occupancy rate of 90%. The average duration of hospitalization is five days and the median rate of CD4 at admission 79 cells/µl. We present here the results of an audit of the management in search of factors on which we could act to reduce mortality.

Objective

Identify modifiable risk factors in the management of patients hospitalized with KHC.

Method

Audit of 208 inpatient records from January 1, 2016 to March 31, 2017, selected according to the following criteria: Primary or secondary diagnosis: tuberculosis, PCP, toxoplasmosis, non-tuberculose pneumonia. CD4 count <200 cells / µl.

The data were collected by a CHK clinician in an Excel database and then analyzed with Stata14.0 The diagnostics check was conducted by a team of clinicians responsible for CHK hospital activities based on MSF algorithms and WHO guidelines.

We assessed the frequency of actual diagnoses according to these definitions and compared the clinical status at admission of deceased patients to those discharged alive, as well as the initiation times of treatments and assessments to determine factors associated with death, using logistic regression.
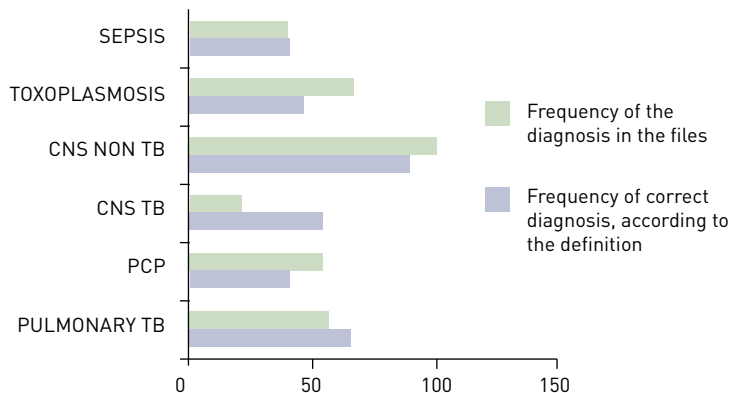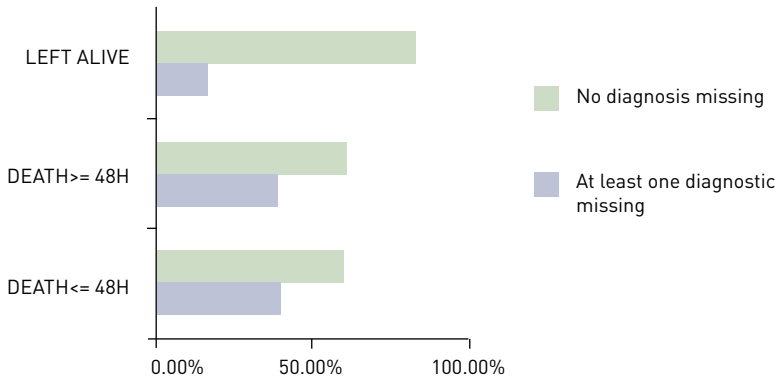
Results

Figure 1: Difference between case diagnoses and actual diagnoses, according to the definition, where TB = Tuberculosis, CNS = central nervous system, PCP = pneumocystosis

Figure 2: Percentage of missed diagnosis by outcome

Table 1: Signs of danger present at admission according to the outcome

Frequency of Signs of Danger	Deaths (120)	Living (88)	P-value
TAS<90	42 (35%)	12 (14%)	0,001
Saturation<90	19 (16%)	6 (7%)	0,048
Inability to walk	77 (64%)	26 (30%)	0,000
At least two danger signs	79 (66%)	35 (40%)	0,000

Management of the most common pathologies

1. **Tuberculosis:** 115 Tuberculosis diagnoses during hospitalization as a primary or secondary diagnosis. The main diagnoses are disseminated tuberculosis, pulmonary tuberculosis, meningeal tuberculosis and abdominal tuberculosis. The median time to start TB treatment is two days in all patients. This delay influences death after 48h in patients with CD4 <50 (p = 0.046). Tuberculosis death is related to CD4 count when CD4 is <50cell / μl (p = 0.036).

2. **Pneumocystosis**: Fifty-five (85.4%) empirical diagnoses and seven (12.7%) radiological diagnoses were made, of which the mode of confirmation is missing. 45/55 (83.6%) cases of PCP received corticosteroids within a median of 24 hours however 41 or 74.5% died. There is a significant difference in the 2-day treatment start-up time (IQ1-3) among the

deceased compared with 1 day (IQ 1-1) in the living, p <0 =, 0212.

3. **Toxoplasmosis**: 67 toxoplasmosis diagnoses with a median treatment start-up time of 1d (IQ 1-3) with no difference between the deceased and the living. 43/67 deaths or 64.1%.

Conclusion

Mortality remains high in hospitalized patients with advanced HIV. This is mainly due to the low rate of CD4 on admission. Tuberculosis is the most common diagnosis and the leading cause of death. CNS tuberculosis is underdiagnosed. Missed diagnoses and time to initiation of tuberculosis and PCP treatment are associated with higher mortality. Early empirical treatment of TB and PCP pneumonia could reduce advanced HIV-related mortality.