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PS1.001

Predictors of late diagnosis of HIV among HIV positive adults coming for initial CD4 T-cell count to public health facilities, Northern Ethiopia

M. B. Beyene[1] and H. B. Beyene[2]

[1]*Epidemiology and Biostastistics, Bahir Dar University, Bahir Dar, Ethiopia;* [2]*Microbiology, Immunology and Parasitology, Addis Ababa University, Addis Ababa, Ethiopia*

INTRODUCTION Early HIV testing and timely initiation of ART decrease mortality and morbidity due to HIV AIDS and improves the quality of life of of people living with HIV. Despite an increased access to HIV/AIDS testing and treatment services late diagnosis is still a problem. Having identified a higher rates of Late HIV diagnosis, this study was aimed to determine determinants of late diagnosis of HIV among adult HIV patients presenting to Bahir Dar Felege Hiwot Referal Hospital in Bahir Dar, Northern Ethiopia.

METHODS An institution-based unmatched case-control study was conducted between January 2010 to December 2011 at Bahir Dar Referral Hospital. A risk set sampling in (1:1) ratio was used to select a sample of 534 clients (267 cases and 267 controls). Cases were adult people living with HIV/AIDS whose initial CD_4 T cell count was <200/μl of blood. Controls were those with a CD_4 T cell count of >200/μl. Trained staff nurses were involved in data collection using a semi-structured questionnaire. Data were entered and analyzed using SPSS version 20. Descriptive statistics and Binary logistic regression were performed.

RESULTS A total of 267 cases and 267 controls were studied. Subjects who hold a certificate and above (AOR = 0.26; 95% CI = 0.13–0.54), being initiated by friends, families and other socials to undertake HIV testing (AOR = 0.65; 95% CI = 0.29–1.48), who reported a medium and high knowledge score about HIV/AIDS and who undertake HIV testing while visiting a clinic for ANC (AOR = 0.40; 95% CI = 0.19–0.83) were less likely to be diagnosed late. Subjects who undertake HIV testing due to providers' initiation (AOR = 1.70; 95% CI = 1.08–2.68), who reported a medium internalized stigma (AOR = 4.94; 95% CI = 3.13, 7.80) and who reported a high internalized stigma score towards HIV/AIDS (AOR = 16.64; 95% CI = 8.29–33.4) had a high odds of being diagnosed late compared to their counterparts.

CONCLUSION Level of education, reason for undertaking HIV testing, knowledge about HIV/AIDS and internalized stigma were significantly associated factors with late diagnosis of HIV. Hence, education about HIV/AIDS particularly towards Testing and ART should be a priority. People should be taught to encouraged and motivate their social mates to undertake HIV testing timely. Organizations working on HIV/AIDS should pay attention to minimizing stigma on HIV/AIDS.

KEYWORDS Predictors, Late diagnosis, HIV/AIDS, Northern Ethiopia.

DISCLOSURE We authors declare that we have no conflict of interest.

PS1.002

Asymptomatic malaria and associated factors among school children in Pawe District, Northwest Ethiopia

H. B. Beyene and N. F. Telele

Microbiology, Immunology and Parasitology, Addis Ababa University, Addis Ababa, Ethiopia

INTRODUCTION A wide scale implementation of malaria control activities in recent years has resulted in a decline of malaria transmission, morbidity and mortality in many African countries. Ethiopia's plan is now to eliminate malaria from selected endemic areas by 2020. Asymptomatic carriage in endemic areas would pose a significant challenge for malaria elimination program. Therefore, the objective of this study was to determine the prevalence of asymptomatic malaria and associated risk factors among children in Pawe Town, northwest Ethiopia.

METHODS AND MATERIALS A cross-sectional study was conducted from January to March 2011. A proportionate systematic random sampling technique was used. A Pretested questionnaire was used to collect sociodemographic data. Capillary blood was then collected from each child. Thick and thin blood films were prepared and stained with Giemsa solution. Diagnosis of malaria and quantification was made by microscopic examinations. Data were entered and analyzed using SPSS 20.0 software. Bivariate and Multiple logistic regression were employed for assessing associated risk factor. A *P*-value < 0.05 was taken as statistically significant.

RESULTS A total of 406 school children were included in this study. A 182 (45%) were females and 224 (55%) were males. The prevalence of asymptomatic malaria among children was 22/406 (5.3%). Of this 19/22 (86%) had low parasite count. *Plasmodium falciparum* infection accounted for 15 (68%) of all positive cases. The prevalence of malaria among 6–15 year-old children was higher than that among those who were older than 15 years ($P = 0.002$). Grade level, age, reported recent intake of artemether-lumefantrine, bed net utilization, and proximity to river were associated with risk of asymptomatic malaria.

CONCLUSION Asymptomatic malaria carriage rate was high among the studied population. Individuals with asymptomatic parasitemia are likely to be most responsible for the ongoing transmission of malaria, because they do not receive treatment and can continue producing gametocytes for a long time. Indeed, to control malaria, all infections must be treated.

DISCLOSURE Nothing to disclose.

aged 12–60 months with uncomplicated malaria were selected and treated with the recommended first line treatment, artemether-lumefantrine (AL) in Uganda and artesunate-amodiaquine (ASAQ) in DRC and followed up for 42 days. In a randomized clinical Trial (RCT), following a 2:2:1 ratio, eligible clinical failures were randomised to either ASAQ, AL or QnC. The outcome was assessed following WHO 2003 criteria. Data were pooled as retreatment or per regimen.
RESULTS Of the 2115 enrolled in the Pre-RCT, 571 were enrolled in the RCT after failing to ASAQ (DRC: 242) or AL (Uganda: 329). Among them 518 (90.7%) were assigned an efficacy outcome. The risk of crude treatment failure was lower after retreatment with an alternative ACT (42.9%, 97/228, HR = 1.6; 95% CI: 1.0–2.5, $P = 0.03$) and may also be lower after retreatment with the same ACT (38.1%, 82/215, HR = 1.5; 95% CI: 0.9–3.1, $P = 0.13$). When assessing per molecules, the risk of failure after treatment with ASAQ was 38.2% (78/204, HR = 1.5; 95% CI: 0.9–2.3, $P = 0.10$) and 42.5% for AL (97/228, HR = 1.6; 95% CI: 1.0–2.5, $P = 0.04$). Risk factors for crude failure were lack of mosquito net ($P = 0.001$) and treatment with AL ($P = 0.01$). After PCR-adjustement (only DRC), all treatments showed a similar efficacy with 7.0% (6/86), 9.3% (9/97, HR = 1.3; $P = 0.61$) and 11.4% (4/35, HR = 1.5; $P = 0.56$) recrudescence for ASAQ, AL and QnC respectively. Alternative ACT showed less drug-related adverse events ($P < 0.001$). AL was better tolerated, compared to QnC ($P < 0.001$) and ASAQ ($P < 0.001$). No serious adverse events were reported in the RCT phase.
CONCLUSION QnC had lower risk of crude treatment failure compared to an alternative ACT. With observed treatment, QnC had thus higher prophylactic effect. After PCR adjustment -only in DRC available- recrudescence rate was comparable between all rescue treatments. NCT01374 581.
DISCLOSURE Nothing to disclose.

PS1.034

Uncomplicated malaria features and efficacy of artesunate-amodiaquine after 42 days of passive follow up in the Democratic Republic of Congo

H. M. Mavoko[1,2], M. Kalabuanga[1], R. Mukele[1], V. Maketa[1,2], B. Fungula[1], C. Delgado[2], R. I. da Luz[2], P. Lutumba[1] and J.-P. Van Geertruyden[2]
[1]*University of Kinshasa, Kinshasa, The Democratic Republic of the Congo;* [2]*University of Antwerp, Antwerp, Belgium*

BACKGROUND In the Democratic Republic of Congo, artesunate-amodiaquine (ASAQ) and artemether-lumefantrine (AL) are recommended as first line treatment, but ASAQ is commonly used. We describe malaria features in Kinshasa and also constitute a cohort for a randomized clinical trial (RCT) to assess efficacy of ASAQ, AL and quinine + clindamycin as rescue treatment.
METHODS Patients aged between 12 and 60 months with uncomplicated falciparum malaria were treated with ASAQ and followed up for 42 days. During follow up, blood smears were only performed when patients were clinically suspected for malaria relapse and at completion. To distinguish new infections from recrudescent parasites, samples were genotyped using a stepwise strategy with up to three molecular markers (GLURP, MSP2 and MSP1). PCR-uncorrected and corrected day-42 cure rates were assessed. Multiplicity of infection (MOI) at individual and population level was assessed by the number of alleles detected on each sample.
RESULTS In total 2796 patients were screened of whom 49.9% were malaria positive. 866 were enrolled of whom 496 (57.3%) were sick at least once during the previous 2 months. Apart from (history of) fever (100%), clinical features were characterized by flu (59.9%) and weakness (59.4%). Geometric mean of parasite load was 230 007 (95% CI: 21 047–25 149). No clinical failure occurred before day 14. Crude efficacy of ASAQ was 55.9% (95% CI: 52.4–59.5) but PCR-adjusted efficacy was 92.8% (95% CI: 90.9–94.6). 83.3% of the recurrences were new infections. Lower mean parasitaemia at enrolment was correlated with crude failure ($P = 0.003$) but not with recrudescence. Low hemoglobin at recruitment was predictor of failure ($P = 0.001$). Polyclonal infections were more frequent (88.1% on day 0 and 80.1% in recurrences) compared to monoclonal infections ($P = 0.005$). The median MOI of recurrence samples (MOI = 3; IQR: 1–5) were lower than the MOI for day 0 samples (MOI = 3.7; IQR: 0.7–6.7; $P < 0.001$). Polyclonal infections were more often in pre-treatment samples than recurrences (OR: 1.8; 95% CI: 1.20–2.8).
CONCLUSION PCR-corrected efficacy of ASAQ is still above the required threshold of 90%. However, crude efficacy was relatively low, suggesting a poor prophylactic effect of amodiaquine in the study area. Assessment of AQ resistance profile as well as the consequences of the MOI are needed.
DISCLOSURE Nothing to disclose.

PS1.035

Estimating of the amount of artemether and lumefantrine excreted through breast milk

J. P. Jain[1], S. Ganesan[1], G. Lefèvre[2] and G. Sunkara[3]
[1]*Novartis Institutes for Biomedical Research, Hyderabad, India;*
[2]*Novartis Institutes for Biomedical Research, Basel, Switzerland;*
[3]*Novartis Institutes for BioMedical Research, East Hanover, NJ, USA*

INTRODUCTION Artemisinin based combination therapies (ACTs) are widely used and recommended by WHO as first-line therapy for uncomplicated *P. falciparum* malaria in nursing mothers. However, artemether-lumefantrine (AL, Coartem®) is not recommended for use during lactation (no breast feeding for at least up to 28 days after last dose) as the excretion of AL in breast milk has not been studied. Clinical data on dihydroartemisinin (DHA, metabolite of artemether) suggest clinically insignificant amount of DHA is excreted in breast milk (peak concentration of 35 ng/ml), after 200 mg artesunate oral dose. In the absence of clinical data, the amount of AL excreted into breast milk has been estimated based on the milk-to-plasma drug concentration ratio (M/P ratio) obtained from preclinical studies. Of note, in a pre-postnatal preclinical study there were no developmental changes in rat pups fed exclusively on the milk of mothers who received 50 mg/kg/day of AL (7.1 mg/kg artemether, 42.9 mg/kg lumefantrine) up to day 21 of lactation.
METHODS In rats the M/P ratio was estimated from distribution of radioactivity in mammary gland after oral administration of radiolabelled artemether and lumefantrine. The potential amount of each drug moiety excreted in mother's breast milk in 24 h was estimated by M/P ratio × maternal plasma Cmax concentration × 150 ml/kg/day (volume of milk consumed per day per kg body weight of infant).
RESULTS The maximum M/P ratios observed over 24 h for artemether and lumefantrine were 1.04 and 1.3, respectively. Over the recommended six doses of AL, the mean maximum plasma concentrations of artemether and lumefantrine were 186 ng/ml and 25.7 μg/ml, respectively, in malaria patients.

Based on the M/P ratio and plasma levels of artemether and lumefantrine, the estimated daily cumulative consumption of artemether and lumefantrine by infants through breast milk following recommended AL doses in nursing mothers is 0.03, 5.01 mg/kg, respectively.
CONCLUSION In the current exploratory assessment, estimated amount of artemether and lumefantrine excreted per 150 ml (per day per kg milk consumption by infant) of breast milk is 0.03, 5.01 mg, respectively, which is ~270 and ~10 fold lower than the recommended daily dose (40 mg and 240 mg of artemether and lumefantrine dose respectively) for 5 kg body weight infants.
DISCLOSURE All the authors are employees of Novartis Institutes for Biomedical Research.

PS1.036

Selective sweeps and genetic lineages of *Plasmodium falciparum* multi-drug resistance (*pfmdr1*) gene in Kenya

P. M. Muiruri[1,2], D. W. Juma[1] and E. Kamau[1]

[1]*Malaria Drug Resistance Laboratory, United States Army Medical Research Unit-Kenya (USAMRU-K), Kenya Medical Research Institute (KEMRI)/Walter Reed Project (WRP), Kisumu, Kenya;* [2]*Department of Biochemistry, Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya*

INTRODUCTION Artemether-lumefantrine (AL) has been the first-line treatment for uncomplicated falciparum malaria in Kenya since 2006. AL selects for K76 in *pfcrt* and N86, 184F and D1246 in *pfmdr1* genes in recurring parasites compared to the baseline infections. Microsatellite (MS) analysis of loci flanking genes associated with antimalarial drug resistance has been used in defining the geographic origins and dissemination of resistant parasites. Kenya has diverse malaria transmission intensities with varying malaria endemicities. This study investigated evidence of selective sweep and genetic lineages in *pfmdr1* genotypes selected for by AL in treatment of malaria infections in Kenya.
METHODS AND MATERIALS Parasites (247) from different regions in Kenya (Kisumu, Kisii, Kericho and Malindi) were analyzed for polymorphisms at codons 86, 184 and 1246 in *pfmdr1*. Samples were typed for 8 NMS and 13 MS loci flanking *pfmdr1*.
RESULTS Full data set was obtained in 79% (186) of the samples. Overall, the prevalence of N86 and D1246 was highest at 85.1% and 90.5% respectively. The most prevalent haplotype was NFD at 53.2%, whereas the least prevalent was YFY at 1.1%. Per site, N86 was highest in Kisumu at 92.6% and lowest in Malindi at 65.1%. Kericho had the lowest prevalence of mutant alleles in all the loci whereas Malindi had the highest. Kisumu had the highest prevalence of NFD (63.4%) whereas Malindi had the lowest (29.7%). The mean H_E for NMS was 0.96 (SE 0.005) vs. 0.627 (SE 0.028) for the 13 MS indicating selection. Parasites carrying mutant alleles had reduced H_E compared to the wild type NYD except for NFD. Analysis of parasite genetic lineages is underway.
CONCLUSION Data show a high prevalence of NFD and NYD, difference in genetic diversity between sites and evidence of selection in *pfmdr1* gene that is statistically different between sites. Data indicate parasites are evolving differently in response to AL drug pressure from one region to another suggesting the rate at which AL tolerance will develop in different regions of Kenya might vary.
DISCLOSURE Nothing to disclose.

PS1.037

Safety of artesunate-amodiaquine, artemether-lumefantrine and quinine + clindamycin as rescue treatment of uncomplicated *Plasmodium falciparum* malaria: an open-label, randomized trial in Kinshasa, the Democratic Republic of Congo

Y. Lula[1,2], H. M. Mavoko[1,2], M. Kalabuanga[1], B. Fungula[1], N. N. Yumva[1], T. Lutete[1], R. I. da Luz[2], J.-P. Van Geertruyden[2] and P. Lutumba[1]

[1]*University of Kinshasa, Kinshasa, The Democratic Republic of the Congo;* [2]*University of Antwerp, Antwerp, Belgium*

BACKGROUND Artemisinin-based combination therapy (ACT) is currently the best option for the treatment of uncomplicated malaria. Quinine is recommended for rescue treatment. However, patients are repeatedly treated with the same antimalarial drug and safety information on this practice is insufficient. To bridge this gap, we report safety data from the quinact randomized clinical trial (RCT) that was designed to assess efficacy and safety of ASAQ, AL and quinine + clindamycin as rescue treatment after ASAQ treatment.
METHODOLOGY The trial was conducted in 3 phases with an informed consent for the 2 first. Males and females aged 12–60 months with uncomplicated malaria were treated with ASAQ and followed up for 42 days (pre RCT). Clinical failures were randomized to the mentioned treatments and followed up for 28 days (RCT). ASAQ was repeatedly used for subsequent failure (post RCT) until a 28-days follow up period without parasitaemia. The adverse events (AEs) were grouped according to the WHO adverse reaction terminology. Causality and severity assessment were done following WHO criteria.
RESULTS 866, 242 and 64 patients were recruited pre RCT, RCT and post RCT respectively. Pre RCT, 433 (50%) patients experienced at least one drug-related AE. The most reported AEs were anorexia (23.6%), asthenia (20%), and abnormal behavior (15%). Twenty nine AEs (3.5%) were reported to be severe. In RCT, at least one drug-related AE was reported in 57.7%, 21.5% and 40% of patient randomized respectively to ASAQ, AL and Quinine + clindamycin ($P < 0.001$). AL was the best tolerated, except for gastro-intestinal disorders. Post RCT, 51.6 patients experienced at least one drug-related AE. Three serious adverse events occurred during the trial, but none of them was related to study medication.
CONCLUSION The proportion of AEs occurrence did not increase over the treatment courses with ASAQ. However, continuous safety monitoring is important.
DISCLOSURE Nothing to disclose.

PS1.038

How is *Plasmodium falciparum* parasite invitro growth fitness affected by drug resistance associated Pfcrt mutations?

B. Aydin Schmidt[1], A. Björkman[1] and G. Fröberg[1,2]

[1]*Microbiology, Tumor and Cellbiology, Karolinska Institute, Stockholm, Sweden;* [2]*Infectious Disease Clinic, Karolinska Institute University Hospital, Stockholm, Sweden*

INTRODUCTION Development and spread of *P. falciparum* malaria parasite resistance to commonly used antimalarial drugs is a major obstacle to achieve elimination. Several questions remain concerning the risk of selection of genetic alterations associated with resistance and how such alterations effect the parasite growth (fitness). We have performed an *in vitro* study