Recurrence of cervical intra-epithelial lesions after thermo coagulation in HIV+ and HIV- Nigerian women


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Background: Cervical cancer remains a leading cause of morbidity and mortality globally. Prevalence of Cervical Intraepithelial Neoplasms (CIN) is between 6-8% in Nigeria; with ~10% of high grade lesions progressing to cancer if untreated. HIV infection may play a role in the recurrence of cervical Intraepithelial lesions following treatment. Screening programs utilizing Visual Inspection with 5% Acetic Acid (VIA) or Lugol’s Iodine (VILI) followed by thermo-coagulation (or cryotherapy) for positive lesions are considered viable options for low-resource settings because of cost and practicability. Studies of recurrence following thermo-coagulation in low-resource settings are scarce.

OBJECTIVES: To investigate the factors associated with recurrence of VIA or VILI positive lesions following treatment with thermo-coagulation in HIV positive and HIV negative Nigerian women.

Methods: A retrospective cohort study of women who were screened in the cervical cancer “see and treat” program of the Institute of Human Virology Nigeria was conducted. We collected data from 5 sites over 4 years in Nigeria: National Hospital Abuja, University of Abuja Teaching Hospital, Garki Hospital Abuja, Federal Medical Centre Keffi and Mother and Child Hospital, Ondo. Inclusion criteria were age ≥18years, baseline HIV status known, VIA/ VILI positive and had thermo-coagulation. We performed logistic regression to examine the proportion of women who returned for scheduled follow-up, those with recurrence and factors associated with recurrence. Ethical clearance was obtained from the Institutional Review Board (IRB) of the University of Maryland Baltimore and the National Health Research Committee (NHREC) of Nigeria.

Findings: Overall, 5,190 women were screened, 7.7%(398/5190) of these were VIA/VILI positive. 65.8%(262/398) had thermo-coagulation (109 were ineligible for thermo-coagulation, 17 did not consent). 67.6%(177/262) were followed up for at least 6 months. Of the 177 included in study, 67.8%(120/177) were HIV positive and 32.2%(57/177) were HIV negative; Mean age (SD) was 34.9 (7.4) years and median follow up time was 531 days (IQR = 673). Recurrence occurred in 16.4%(29/177) of participants and was higher in HIV positive women (18.3%) compared to HIV negative women (12.3%) but this was not statistically significant (p-value 0.31). Women aged ≥30 years were much less likely to develop recurrence, OR = 0.28 (95%CI = 0.12, 0.65). Among HIV positive women, CD4 cell count < 200cells/mm3 was associated with recurrence, OR = 3.68 (95%CI = 1.15, 11.7).

Interpretation: Recurrence of VIA/ VILI positive lesions after thermo-coagulation occur in a significant proportion of women. A high proportion of VIA/VILI positive women did not return for follow up visits highlighting the challenge of effective screening programs in this population and the need to continue research into most appropriate screening strategies. HIV positive women with low CD4 counts are at increased risk of recurrent lesions and may be related to immunosuppression.

Maternal obesity in Africa: Is it time to pay more attention?

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Background: Many African countries are experiencing a double burden of under- and over-nutrition due to factors such as globalization, urbanisation, changing diet, and cultural perceptions of weight. Pregnancy is a trigger point for the development of obesity, and maternal obesity is associated with short- and long-term adverse effects in the mother and child. However, while the effects of maternal under-nutrition are well known and addressed, there is scarcity of data on maternal obesity in African countries. Nigeria, Africa’s most populous country is experiencing rising levels of obesity and efforts to prevent and manage obesity in pregnancy are urgently needed in Nigeria. The study aimed at identifying the components of an intervention for maternal obesity in Nigeria which may be subsequently adapted to similar African countries. The objectives were to assess the prevalence, effects and distribution of maternal obesity; assess the knowledge, attitude and practice of pregnant women and maternal healthcare providers and identify existing interventions for maternal obesity.

Methods: A systematic review and meta-analysis on maternal obesity in Africa was conducted. Following on the results of this review, a cross-sectional observational study utilising both quantitative and qualitative research methods was done. For the cross-sectional study, eight hospitals across Nigeria were selected via multi-stage random sampling. A questionnaire survey of pregnant women and semi-structured interview of maternal health care workers was conducted. Data from the questionnaire survey is being analysed with SPSS using appropriate tests while thematic analysis is being conducted for the interviews.

Findings: Twenty-nine studies were included in the systematic review. Prevalence of maternal obesity across Africa ranged from 6.5% to 50.7%, using body mass index and weight measurements at different gestational ages. Pregnant women who were older, urban dwellers and had higher parity were more likely to be obese than non-obese. Meta-analysis showed increased odds of adverse maternal and child outcomes for obese pregnant women. However, newborns with significantly lower birth weight were more likely to have non-obese mothers than obese mothers. Questionnaires were completed by 474 pregnant women, and twenty-two health care workers were interviewed until data saturation. Data analysis is presently being conducted. Emerging themes from qualitative study show that barriers to achieving ideal weight in mothers include booking for antenatal care late in pregnancy, and insufficient knowledge on the management of maternal obesity by health care workers.

Interpretation: Culturally adaptable/sensitive interventions should be developed for the management of obese pregnant women in Africa. Education and training of health care workers on efficient and effective interventions may assist health workers in ensuring women are supported to provide optimal maternal and infant health outcomes.
Addressing severe acute malnutrition and anemia in Charnia, Haryana, India

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Program/Project Purpose: Severe acute malnutrition and anemia (SAMA) are major causes of maternal and infant mortality in rural India. India’s health system faces challenges in tackling the rapidly escalating burden of SAMA due to limited access to healthcare facilities, pervasive poverty, and inadequate infrastructure to effectively treat the population. Upon conducting extensive needs assessments and hemoglobin testing in Charnia, Haryana, India, we found anemia and malnutrition prevalence to be high with over 80% of children and 100% of pregnant women tested in Charnia having hemoglobin levels indicative of anemia. Thus, our primary focus was to analyze the methods of sustainably mitigating anemia rates in rural Charnia, Haryana, India through a community health worker (or health promoter) program.

Structure/Method/Design: We performed baseline hemoglobin testing and distributed IFA and Albendazole (deworming) to women and children. The mean hemoglobin level of the 113 individuals tested was 10.08 g/dL, and the prevalence of anemia was 78.8%. Accordingly, we trained health promoters for the experimental group. These individuals were expected to encourage anemia awareness and IFA compliance in their communities. Furthermore, Charnians have a very plain diet consisting primarily of rice, lentils, and potatoes. Lack of a varied diet and general malnutrition only compounds the anemia issue in Charnia. This short-term anemia intervention was conducted focus group sessions with community health workers (ASHAs) and develop tools to assist ASHAs. Through the focus groups, we found the ASHAS to be open to additional trainings, novel approaches to treating SAMA, and open to implementing mobile health tools in their workflow.

Outcomes & Evaluation: The results of the intervention demonstrated that the government’s delivery system must be improved for community participation; increased oversight of the health promoters is necessary; and an IFA intervention must be combined with long-term food-based approaches to promote sustainability. However, to target long-term behavior change interventions in Charnia, we conducted focus group sessions with community health workers (ASHAs) serving the Charnia area to better understand barriers facing ASHAs and develop tools to assist ASHAs. Through the focus groups, we found the ASHAS to be open to additional trainings, novel approaches to treating SAMA, and open to implementing mobile health tools in their workflow.

Going Forward: Moving forward, we are collaborating with the George Institute for Global Health to develop a smart phone tool that will train healthcare workers in Charnia to assess, refer, and/or treat individuals with anemia and malnutrition. (Unpublished Data, Northwestern Project RISHI, Rural India Social Health Improvement).

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Interrogation of HHV-8 transcriptome in KS tumors and association with KS presentation and outcomes in Uganda

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Background: Kaposi sarcoma (KS) is the most common HIV-associated malignancy worldwide and among the most frequently diagnosed cancers in several African countries, where KS prognosis remains poor. Discovery of new KS biomarkers that improve current staging systems or identify new molecular targets for treating KS could significantly improve outcomes. In vitro work suggests that human herpesvirus-8 (HHV-8) produces several angiogenic, inflammatory, and immunomodulatory gene products that contribute to KS pathogenesis, but data on the expression of HHV-8 genes in vivo remain limited. To identify candidate biomarkers and therapeutic targets, we sought to characterize HHV-8 gene expression in KS tumors of Ugandan adults and to correlate the expression of HHV-8 gene transcripts with KS clinical presentation and outcomes.

Methods: KS tumor biopsies were obtained from treatment-naïve HIV-infected adults with histologically-confirmed KS initiating therapy at the Uganda Cancer Institute in Kampala, Uganda. KS samples were stored in RNAlater or flash-frozen and stored in liquid nitrogen; HHV-8 mRNA transcripts were quantified using RNA-Seq.

Findings: 48 participants contributed 48 KS biopsies. 11 (23%) participants were women, and the mean age was 34 years (range 21-61 years). The median baseline CD4 T-cell count was 187 cells/mm3 (IQR 53, 352 cells/mm3), and median baseline plasma HIV-1 RNA level was 5.5 log10 copies/mL (IQR 5.0, 5.8 log10 copies/mL). The KS biopsies represented a range of tumor morphotypes, including 28 (58%) macular, 18 (38%) nodular, and 2 (4%) fungating lesions. All participants received treatment with ART and chemotherapy; 35 (73%) achieved a partial response, and 13 (27%) had progressive disease or died within the first 4 months of therapy. Based on analyses completed to date, all biopsies had HHV-8 mRNA gene transcripts detected. Highly expressed transcripts in all samples included the known latent gene products Kaposin, vFLIP, vCYC, and LANA, and the lytic gene products vIL-6, vAP, vCCL-2, bZIP, and ORF75. HHV-8 gene expression differed by tumor morphotype, with nodular lesions expressing higher levels of several lytic genes, including vIL-6 (p = 0.01), vCCL-2 (p = 0.02), and vAP (p = 0.008), compared to macular lesions. High levels of specific genes were also associated with poor survival, including MIR1 (HR = 1.3; p = 0.03), vCCL-2 (HR = 1.3; p = 0.04), and vCCL-1 (HR = 1.3; p = 0.02). Additional RNA-Seq data will be presented for the entire set of biopsies.

Interpretation: KS tumors expressed high levels of both latent and lytic HHV-8 mRNA transcripts. Highly expressed transcripts included several functional genes encoding cytokines (vIL-6), growth regulatory genes (vCYC), and apoptosis inhibitors (vFLIP), and the differential expression of these viral genes appeared to be associated with different tumor types. Importantly, several of these gene products represent potential targets of therapy with available drugs and may serve as candidates for future therapeutic trials to improve KS outcomes.

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The role of HPV testing in reducing the burden of cervical cancer in low and middle income countries

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