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Abstract #: 01NCD029

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 assessed in August, 2014. Of the original 113 participants, only 12 remained in the community. Due to the migratory population, tracking and follow up with the study participants was difficult, and the remaining 12 participants' hemoglobin levels were not tested.

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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Abstract #: 01NCD030

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, vIAP, 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 vIAP (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 (v-CYC), and apoptosis inhibitors (v-FLIP), 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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Abstract #: 01NCD031

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

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Program/Project Purpose: Virtually all cases of cervical cancer are associated with persistent infection of high-risk serotypes of HPV. While cytology based screening programs have significantly reduced the cervical cancer incidence in high income countries they have proven ineffective in low and middle income countries (LMICs). This shortfall appears to be due to a number of factors, including the need for complex laboratory equipment, highly trained staff, informatics and logistics for follow up of results, and availability of treatment. HPV DNA testing may potentially decrease these programmatic requirements and thus presents a pragmatic and advantageous alternative for cervical cancer screening. Due to disproportionately higher rates of cervical cancer incidence and mortality, it is critical to ensure these technological advancements are feasible for LMIC's to utilize in moving past opportunistic screening and towards scaling up cervical cancer screening programs. The World Health Organization (WHO) recently released cervical cancer guidelines recommending HPV testing for screening where resources permit. Ensuring that LMIC's benefit from the new technology requires collaboration and a neutral facilitator for information flow between public and private institutions. In response to this need the National Cancer Institute of the United States Institutes of Health (NCI/NIH) and the Pan American Health Organization (PAHO/WHO) convened industry, representatives of Latin American and Caribbean (LAC) ministries of health as well as experts in the field to discuss testing options and programmatic needs. The meeting HPV testing's Role in Reducing the Global Cancer Burden was held at PAHO on May 12 and 13, 2014.

Structure/Method/Design: It included the participation of eight HPV testing diagnostic companies, representatives from six ministries of health from Latin America and the Caribbean, other U.S. Government agencies like CDC, international organizations including WHO and IARC, PATH and the Gates Foundation as well as U.S. universities working on global health.

Outcomes & Evaluation: Discussion included the implementation of an up scaling process for the region and potential mechanisms available at both PAHO and WHO that could potentially assist to make the test more affordable to Member Countries in the LAC region. Other concrete products of the meeting include the development of a document that summarizes the available HPV tests and their requirements to be used by Ministries of Health and relevant agencies in Latin America and the Caribbean and a Training Manual pertaining HPV Testing for Health Officers in Latin America and the Caribbean that is expected to be ready by early 2015.

Going Forward: The lessons learned from this meeting could be potentially applied to a similar initiative in other LMICs region including Africa and Asia.

Funding: Costs were shared between the NCI and PAHO.

Abstract #: 01NCD032

Single nucleotide polymorphisms of the renin angiotensin system linked to high prevalence of essential hypertension in the Taita tribe of Kasigau, Kenya

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Background: The rapid growth of chronic non-communicable disease (CNCD), in particular cardiovascular disease, is a significant problem in developing countries. The World Health Organization

(WHO) estimates that in 10 years global CNCD deaths will increase by 17% with the greatest increase (27%) being in Africa. Essential hypertension (EH) is a leading risk factor for vascular diseases such as stroke, myocardial infarction, and heart failure. Although managing EH in developing countries is considered a high global priority, few epidemiological and/or genetic studies exist from third world populations. As a part of Western Kentucky University's Partners in Caring: Medicine in Kenya (PiC:MiK) program, we have been able to investigate the allele frequency of five different polymorphisms of the renin-angiotensin system (RAS), the key hormonal pathway that regulates blood volume and salt, from a rural cohort of Kenyans primarily of the Taita tribe, and subsequently, evaluate the relationship between these polymorphisms and EH.

Methods: A cross-sectional study of ~200 participants was conducted using genomic DNA isolated from buccal cells and amplified by PCR with the fluorescent-based TaqMan™ SNP genotyping assay. The polymorphisms evaluated were angiotensinogen (AGT) M235T, angiotensin II receptor Type 1 (AGTR1) A1166C, hydroxysteroid(11β)dehydrogenase (HSD11β2) C534A, aldosterone synthase (CYP11B2) C344T, and the angiotensin (ACE) insertion/deletion (I/D) polymorphism.

Findings: We have determined the genotype distribution for each polymorphism as follows: AGT C/C= 0.63, C/T= 0.34, T/T= 0.03; AGTR1 A/A= 0.96, A/C = 0.03, C/C= 0.0; HSD11b2 A/A = 0.46, A/C=0.46, and C/C=0.08; and CYP11B2 T/T=0.66, T/C = 0.30, C/C =0.30. Overall, there was an over-representation of the AGT susceptible C allele and the ACE D allele.

Interpretation: In this cohort, the high prevalence of two alleles previously linked to an increased predisposition for EH, suggests they likely are an important factor driving the common occurrence of EH observed in the people of Kasigau, Kenya. To our knowledge our results are the first to identify allelic frequencies in RAS in East Africans of Taita origin. Currently, statistical analyses to correlate genotype frequencies to relative risk of EH are being conducted.

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Abstract #: 01NCD033

Prevalence of depression, substance abuse, and stigma among men who have sex with men in coastal Kenya

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Background: Mental health conditions can have a severe impact on quality of life and interfere with health-related behaviours such as medication adherence. Our aim was to determine the prevalence of depression, substance abuse, and stigma among self-identified men who have sex with men (MSM) in coastal Kenya.

Methods: A cross-sectional study was conducted at the Kenya Medical Research Institute's HIV/STD clinic in Mtwapa, Kenya. Participants were 112 self-identified MSM involved in ongoing cohort studies, who had consented to collection of health-related data. We used audio computer-assisted self-interview (ACASI) to collect data on the following psychosocial measures: depression (PHQ-9), alcohol use (AUDIT), other substance use (DAST), sexual stigma (modified China MSM Stigma Scale), HIV stigma (modified