Methods We conducted qualitative interviews with 30 PLHIV with hazardous alcohol use from an antiretroviral therapy (ART) clinic in the Thai Nguyen to inform item development. Alcohol use was assessed using the Alcohol Use Disorders Identification Test (AUDIT). We tested items in a quantitative survey of 1,559 ART clinic patients in Thai Nguyen to assess internal reliability (Cronbach’s α) and structural validity (exploratory factor analysis, EFA). We used binomial logistic regression to estimate associations between AAS (median score >7) and alcohol use.

Results Using the results from the qualitative interview data, we developed the AAS scale with seven final items covering internalized, experience, and anticipated stigma, with scores ranging from 7 to 35. The scale had good internal consistency (α=0.75). EFA suggested the presence of two factors (r=0.42) that explained 64.5% of the total variance. Overall, the median AAS score was 7 (IQR:7–11). Those with alcohol dependence symptoms (AUDIT≥20) reported higher levels of AAS (median=9, IQR:7–14) and non-harmful alcohol users (AUDIT<8) reported lower levels of AAS (median=7, IQR:7–9). AAS was significantly associated with alcohol dependency, (adjusted prevalence ratio APR =1.74, 95%CI: 1.53;1.99), adjusting for age, gender, and employment status.

Conclusion The AAS scale may be utilized or adopted to measure alcohol abstinence stigma among PLHIV in settings where alcohol use is culturally encouraged. This new measure will aid future studies assessing the value of developing culturally sensitive strategies to reduce alcohol consumption and ultimately improving HIV treatment outcomes among PLHIV.

Disclosure No significant relationships.

015.6 WOMEN’S APPROACHES TO INVOLVING OTHERS IN MAKING HIV TRIAL ENROLLMENT DECISIONS WHILE PREGNANT IN THE US AND MALAWI

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Background There is a pressing need to expand the HIV prevention and treatment evidence base in pregnancy. However, research in pregnancy entails unique ethical and scientific complexities. The decision-making processes of potential trial participants in the doubly sensitive context of HIV, a highly stigmatized disease, and pregnancy, where multiple stakeholders and sociocultural practices may influence women’s preferences, are not well understood. Involvement of others in decision-making processes may vary, including who pregnant women consult and why, and the influence of consultations on decisions. Understanding women’s involvement of others in participation decisions is critical to inform practices supporting informed decision-making.

Methods 140 in-depth interviews were conducted with pregnant or recently pregnant women; 70 in the U.S. and 70 in Malawi, 35 HIV-positive and 35 uninfected in each setting. Participants described whether they would involve others in enrollment decisions while pregnant for hypothetical HIV prevention or treatment research scenarios. Thematic analysis informed the analytic approach. Interviews were transcribed, translated when necessary, coded, and emergent themes identified.

Results In both contexts, many women described collaborative decision-making approaches, particularly with male partners, female relatives and friends, and in the US, clinicians. Participants commonly described valuing others’ perspectives on risks and benefits and shared responsibility for the decision. Many women described sole decision-making authority, even if informing others was likely or necessary. Few women
THERAPEUTIC EFFECT OF INDOLEAMINE 2,3-DIOXYGENASE (IDO) INHIBITOR IN THE MALE GENITAL INFLAMMATION

Background Indoleamine 2,3-dioxygenase (IDO) catalyzes the first and rate-limiting step of tryptophan catabolism.IDO is induced in various tissues during systemic infection and plays a key role in immune response. Therapeutic effect of IDO inhibitor for systemic infection was already reported, but the effect for local infection was still unclear. We hypothesize that IDO play a central role for local immunological reaction in the male genital inflammation and IDO inhibitor contribute to innovative therapy for the male genital inflammation. To validate this hypothesis, we inhibited IDO using 1-methyltryptophan (1-MT) and investigated inflammatory changes in the male genital inflammation model.

Methods Twelve weeks old C57BL/6 male mice were used through the study. 1-MT 100μg was intraperitoneally administrated and confirmed inhibitory effect of 1-MT. Lipopolysaccharide (LPS) 100μg was injected to the male genitalia (epididymis and prostate) and confirmed validity of modeling. Based on the results of preliminary examination, LPS was injected three hours after 1-MT administration. After modeling, male genitalia were removed in a time-dependent manner. Inflammatory changes were analyzed using comprehensive cytokines/chemokines assay and immunohistochemical changes were analyzed using representative candidates.

Results Histological analysis showed that invasion of inflammatory cells and destruction of ductal structure were observed in the male genital inflammation model of 1-MT(-) mice compared with that of 1-MT(+) mice. Comprehensive cytokines/chemokines assay showed that down-regulated expression of inflammatory promoting cytokines/chemokines (epididymitis: IL-1α, IL-6, CCL3, CXCL1, Prostatitis: IL-16, TREM-1, CXCL10, CXCL12) were observed in male genital inflammation model of 1-MT(+) mice compared with that of 1-MT(-) mice. Same results were obtained from separate quantitative assay and immunofluorescent staining.

Conclusion Ido is involved in immunological reactions via cytokines/chemokines in the male genitalia. Inhibition of Ido may contribute to protection of the male genital inflammation. Therefore, Ido inhibitor might be a novel target therapy for the male genital inflammation.

Disclosure No significant relationships.

O16 – HOST-PATHOGEN INTERACTIONS

Wednesday, July 17, 2019
1:45 PM – 3:15 PM

O16.1 THERAPEUTIC EFFECT OF INDOLEAMINE 2,3-DIOXYGENASE (IDO) INHIBITOR IN THE MALE GENITAL INFLAMMATION

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Background Indoleamine 2,3-dioxygenase (IDO) catalyzes the first and rate-limiting step of tryptophan catabolism. IDO is involved in immunological reactions via cytokines/chemokines in the male genitalia. Inhibition of Ido may contribute to protection of the male genital inflammation. Therefore, Ido inhibitor might be a novel target therapy for the male genital inflammation.

Disclosure No significant relationships.

O16.2 MAPPING REGIONS OF HOST ATTACHMENT IN THE T. pallidum ADHESIN TP0751: FUNCTION-INFORMED VACCINE DESIGN

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Background Treponema pallidum spp. pallidum (T. pallidum), the causative agent of syphilis, is a highly invasive pathogen that moves throughout the body via the bloodstream and invades every organ and tissue to cause the serious sequelae associated with sexually-transmitted and congenitally-acquired syphilis infections. Prevention of pathogen spread via the bloodstream is a critical requirement of a successful syphilis vaccine. The T. pallidum vaccine candidate Tp0751 is a host-binding adhesin that interacts with endothelial cells lining blood vessels. In this study we identify epitopes of Tp0751 that, when blocked with neutralizing monoclonal antibodies (mAbs), interrupt host endothelial cell interaction. This improved understanding will enhance antigen selection for syphilis vaccine development.

Methods Epitope localization of mAbs specific for Tp0751 was completed via enzyme-linked immunosorbent assays using several truncated versions of Tp0751. Following epitope localization, recombinant Tp0751 was incubated with individual mAbs and subsequently assayed for inhibition of Tp0751 adhesion to endothelial cells compared to that observed using control antibodies.

Results Epitope screening of Tp0751-specific mAbs identified functionally important regions of Tp0751 that mediate adherence to host cells. Inhibition studies revealed that all mAbs reactive against a defined C-terminal structural domain of Tp0751 impeded adherence of recombinant Tp0751 to endothelial cells. In contrast, N-terminal-reactive mAbs did not display this inhibition. These molecular studies allowed localization of neutralizing epitopes within a functionally important domain of the Tp0751 adhesin, which in turn assists with informed vaccine design.

Conclusion This study identified epitopes of Tp0751 that are important for T. pallidum host cell adhesion. Host immune targeting of these functional regions may facilitate antibody-dependent neutralization of treponemal dissemination, which is needed to establish protective immunity against T. pallidum. These results further our understanding of T. pallidum host cell adhesion and allow refinement of antigen selection for syphilis vaccine development.

Disclosure No significant relationships.