THE COMPREHENSIVE CERVICAL CANCER PREVENTION IN TANZANIA (CONCEPT) PROJECT

HPV Acquisition

Research update VIII

Partners

The CONCEPT study is an international research collaboration project between Denmark and Tanzania, funded by the Danida Fellowship Centre.

The Tanzanian partners are Ocean Road Cancer Institute (ORCI) and Kilimanjaro Christian Medical Centre (KCMC).

The Danish partners are the University of Southern Denmark (SDU) and the Danish Cancer Society Research Center.

Danida Fellowship Centre
- sustaining development through research and learning

SDU
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ORCI

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Key findings: HPV acquisition

- A sub-study of the CONCEPT cohort was to assess the incidence of high-risk (HR) human papillomavirus (HPV) and associated risk factors for acquisition.
- Overall, incident HR HPV was higher among HIV-positive women compared to HIV-negative women.
- HPV 52, HPV 16 and HPV 35 were acquired more often compared to other HR HPV types, irrespective of the HIV-status.
- Age, being single, multiple sexual partners and lower CD4 Count among HIV-positive women were associated with increased acquisition of HR HPV.

Introduction

This research update describes acquisition patterns of high-risk (HR) human papillomavirus (HPV) among a cohort of Tanzanian women, which was established as part of the research project CONCEPT (***Comprehensive Cervical Cancer Prevention in Tanzania***).

Cervical cancer is the major cause of cancer-related deaths among women in low- and middle-income countries, including Tanzania. Human papillomavirus (HPV) is responsible for virtually all cases of cervical cancer, and HIV-positive women have increased risk of HR HPV compared to HIV-negative. However, controversy prevails regarding the magnitude and risk factors for HPV acquisition among HIV-positive women as most existing evidence mainly stems from high-income countries whilst data from highly HIV prevalent settings - such as Tanzania - is relatively sparse.

Current evidence shows that HIV-positive women have an increased risk of having broader range of high-risk (HR) HPV types compared to HIV-negative. Yet, the majority of data that describe HR HPV acquisition among HIV-positive women have been conducted among adolescent women in HPV vaccination trials with relatively inadequately powered HIV-positive women and shorter duration of follow up (4, 5).

Sexual contact is considered to be the main risk factor for HPV acquisition among young women(6-8). However, incidents HPV cases in sexually inactive older women poses a dilemma in the potential route of acquisition involved. Several postulates have been suggested in the literature regarding this event, including the reactivation of HR HPV from latent infection and inoculation of HP HPV from other anogenital sites(9).

In order to understand the role of sexual and reproductive related factors in incident HPV cases among middle-aged and adult women, a cohort of HIV-positive and -negative women were followed over an average course of 14 months in order to detect changes in their HPV status at the enrollment and during follow up. The research update describes the study that assessed the incidence of HPV and associated risk factors for acquisition among this cohort of women. Specifically, this study aimed to:

1. *To assess the incidence of HR HPV (both general and type specific) over the course of 14 months and determine risk factors associated with HR HPV acquisition among HIV-positive and HIV-negative women*

Methods

Women aged 25-60 years were recruited in routine cervical cancer screening clinics at KCMC hospital and Mawenzi hospital in Kilimanjaro region and Ocean Road Cancer

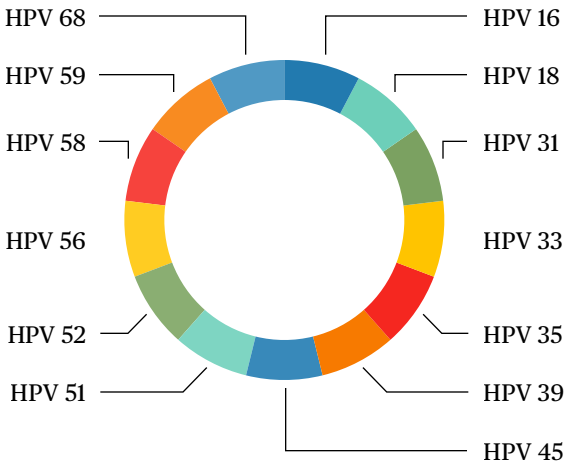
Institute in Dar-es-salaam region. Informed consent was sought prior to enrollment. Women aged 25-60 years, non-pregnant without prior history of cervical lesion were included. Provider-initiated counseling and testing for HIV was offered to all women. In order to obtain relevant socio-demographic, reproductive and sexual characteristics, a structured questionnaire interview was conducted through a face-to-face interview by trained health care providers. This was followed by a gynecological examination where cervical swabs were obtained for liquid based cytology and HPV testing using Hybrid Capture 2(HC2) DNA analyses and genotyping using LiPaExtra. Further, routine cervical cancer screening using visual inspection with acetic acid (VIA) was provided.

A follow-up screening visit was conducted at an approximate duration of 14 months after enrollment. Women were re-tested for HPV a follow-up, responded to a questionnaire and received VIA. A subset of women did not attend the follow-up screening at the clinic but were traced at home, where a HPV self-sample was collected using the Evelyn brush, and VIA was not conducted.

Evalyn self-sample brush

STATISTICAL ANALYSIS

HPV acquisition was defined as the detection of HR HPV - both general and type specific - during a follow-up visit among women who were HR HPV negative at enrollment. The following 13 oncogenic HR HPV types were assessed in the study:



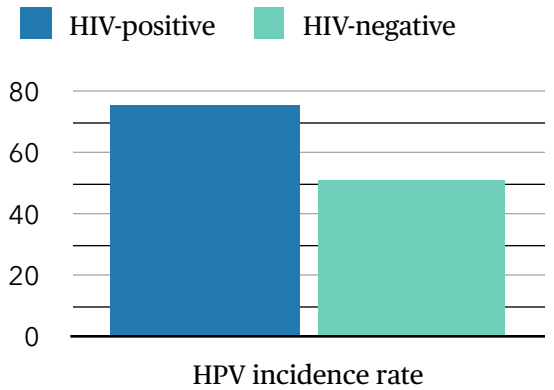
Incidence rates (acquisition of HPV) was estimated as the number of events divided by the person-years at risk. We examined the HR HPV incidence rate according to HIV-status and age. Further, we assessed the incidence of overall and type-specific HR HPV among HIV-positive and -negative women. A logistic regression was used to determine the association of the selected sexual and reproductive factors and the risk of HR HPV acquisition.

Main findings

A total of 4043 women were included in the cohort at baseline, and 5.8% of these women were not legible for follow up visits due to various reasons, such as residence relocation, pregnancy, hysterectomy and death. Among the 3805 women, who were legible for follow-up, a total of 3074 (80.8%) attended a follow-up visit.

A total of 2253 were HR HPV negative at enrollment, and 184 of these women acquired HR HPV during follow-up. This corresponds to an incident rate of 54.5 (95% CI: 47.1-62.9) per 1000 person-years. The incidence rate among HIV-positive women was 75.2 (95% CI: 54.5-103.7) per 1000 person-years and 50.9 per 1000 person-years (95% CI: 43.3-60.0) for HIV negative women.

Incidence rate of HR HPV among HIV-positive and HIV-negative women per 1000 person years



HR HPV incidence decreased with increasing age, irrespective of HIV status. Regarding type-specific acquisition, HPV52 was most often acquired (12.5; 95% CI: 9.5-16.5) followed by HPV16 (6.9 95% CI: 4.8-10.1). Factors associated with HR HPV acquisition included **HIV** (OR 1.7; 95% CI 1.2-2.6), older **age** (OR 0.5; 95% CI 0.3-0.8), **multiple sex partner** (OR 2.9; 95% CI 1.4-5.9). **Low CD4 count** (<199cells/mm^3) among HIV-positive women was associated with increased risk of HR HPV acquisition (OR 5.3; 95% CI 1.9-15.2)

Future perspectives

Overall, incident HR HPV was higher among HIV-positive women compared to HIV-negative women. HPV 52, HPV 16 and HPV 35 were relatively acquired highly as compared to other HR HPV types, irrespective of the HIV status. Age, being single, multiple sexual partners and lower CD4 Count in HIV positive women were the factors associated with increased acquisition of HR HPV.

Interventions designed to reduce sexual risky behavior have a potential to reduce HR HPV incidents in this population. Given the type-specific HR HPV acquired in this study, vaccination with the nonavalent HPV vaccine will reduce incident HPV infections and eventually cervical cancer more effectively.

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