

# Antibodies against high-risk human papillomavirus proteins as markers for noncervical HPV-related cancers in a black South African population, according to HIV status.

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Human papillomavirus (HPV) proteins may elicit antibody responses in the process towards HPV-related malignancy. However, HPV seroepidemiology in noncervical HPV-related cancers remains poorly understood, particularly in populations with a high prevalence of human immunodeficiency virus (HIV). Antibodies against E6, E7 and L1 proteins of HPV16 and HPV18 were measured in sera of 535 cases of noncervical HPV-related cancers (anal (n=104), vulval (n=211), vaginal (n=49), penile (n=37) and oropharyngeal (n=134)) and 6,651 non-infection-related cancer controls, from the Johannesburg Cancer Study that recruited Black South African with newly diagnosed cancer between 1995 and 2016. Antibody response was evaluated using a glutathione S-transferase-based multiplex serology assay. Logistic and Poisson regression models were used to calculate adjusted odds ratios (aOR) and prevalence ratios (aPR) and 95% confidence intervals (CI) in cases versus controls. HPV16 E6 was strongly associated with noncervical HPV-related cancers: anal (females (aOR=11.50;95%CI:6.0-22.2), males (aOR=10.12;95%CI:4.9-20.8), vulval (aOR=11.69;95%CI:7.9-17.2), vaginal (aOR=10.26;95%CI:5.0-21), penile (aOR=18.95;95%CI:8.9-40), and oropharyngeal (females (aOR=8.95;95%CI:2.9-27.5), males (aOR=3.49;95%CI:1.8-7.0)) cancers. HPV16-E6 seropositivity ranged from 24.0% to 35.1% in anal, vulval, vaginal and penile cancer but was significantly lower (11.2%) in oropharyngeal cancer. After adjustment for HIV, prevalence of which increased from 22.2% in 1995-2005 to 54.1% in 2010-2016, HPV16 E6 seropositivity increased by period of diagnosis (aPR for 2010-2016 versus 1995-2006=1.84;95%CI:1.1-3.0). Assuming HPV16 E6 seroprevalence reflects HPV attributable fraction, the proportion of certain noncervical-HPV-related cancers caused by HPV is increasing over time in South Africa. This is expected to be driven by the increasing influence of HIV

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