

Cele L^{1.}, Sebitloane H.M^{1.}, Abbai N.S^{1.}, Forestier M^{2.}, and Almonte M²

1. School of Clinical Medicine, University of KwaZulu-Natal, South Africa. 2. International Agency Research on Cancer (IARC), France.

BACKGROUND

The incidence of cervical cancer (CC) globally is estimated at 500,000 new cases per year. Cervical cancer can be linked with human papillomavirus (HPV), which is found in 99% of cervical cancers. The persistence of HPV, specifically high-risk HPV (HR-HPV) is responsible for the development of CC and its precursor lesions. HPV infection in the cervix causes cervical intraepithelial neoplasia (CIN) and invasive cancer (IC).

HPV infection and health-related regimes influence the progression of CIN. HPV is important to the conversion of the cervical epithelial cells mostly subtype 16 & 18. CIN refers to the changes in squamous cells of the cervix, in which they are precancerous lesion which are associated to cervical invasive carcinoma. The intensive changes (CIN grade 2 or CIN3+) are identified as high-grade squamous intraepithelial lesions (HSIL) and it is estimated that 25% of these women will progress to invasive cancer if left untreated. Majority of the cervical cancer cases arise from less developed countries.

The oncogenic potential of HR-HPV depends on the increased expression of the HPV E6 and E7 mRNA oncogenes. The detection of HPV E6 and E7 oncogene transcripts might serve as an additional factor in the risk evaluation, their presence indicating an increased risk of the development of CIN or the progression of CIN to cervical cancer.

The aim of the study was to determine the role of HPV E6/E7 mRNA in the prevalence and the progression of cervical neoplasia in HR-HPV and human immunodeficiency virus (HIV) positive women.

METHODS

- HIV positive women were recruited from antiretroviral (ARV) clinics in the Durban area, South Africa.
- HPV positive were randomized at 4:1 ratio into HPV +VIA+ treatment (ARM 1) and HPV + Treatment (ARM 2).
- Women in arm 1 received VIA and only positive for VIA was treated.
- In arm 2 all the HPV positive women were treated.
- Women which were eligible for ablative treatment were randomized into treatment with Thermal ablation (TA) or Cryotherapy (Cryo) in both arms and the rest were referred to colposcopy.
- At 1 year follow-up (1yrFU) women were screened with HPV testing and VIA and 2-3 biopsies were taken for colposcopy in all HPV women.
- Women with CIN2/3 and those which were eligible for ablative treatment were randomized into TA or Cryo.
- Women who were CIN 1 or negative were referred back to ARV clinic for routine cervical cancer screening and the rest were referred to colposcopy for appropriate management.
- The E6/E7 test was carried out by using the Arbor vita, Enco6 kit procedure was protocol provided.
- This is cohort study where 377 HR-HPV positive cervical samples (207 baseline and 107 follow-up) were used.

RESULTS

Table 1: The prevalence of CIN and HPV E6/E7 mRNA at recruitment

Variables	N	Percentage
Begnin	25	12.3%
CIN2/3+	178	87.7%
E6/E7 +ve (recruitment)	30	12.5%
E6/E7 -ve (recruitment)	211	87.6%
Begnin (FU)	6	13.6%
CIN2/3+ (FU)	33	86.4%
E6/E7 +ve (FU)	6	14.6%
E6/E7 -ve (FU)	35	85.4%

Table 2: The relation of HPV E6/E7 mRNA and CIN

	CIN result				Total	p value
	Benign (1-2)		3-7			
E/E7 result	n	%	n	%		
0	23	13,5%	148	86,5%	171	0,54
1	2	7,4%	25	92,6%	27	

The study results showed that 86.5% of participants were HPV E6/E7 mRNA negative and had Benign ≤ CIN2 and HPV E6/E7 mRNA positive had ≥ CIN3+ 92.6% but there was no statistical significance (p>0.05).

DISCUSSION AND CONCLUSION

- ❖ Our results were not contrast with previous studies as there was statistical significance in other studies, however our results showed that participant that were HPV E6/E7 mRNA positive had had higher clinical means than those who tested HPV E6/E7 mRNA negative, i.e., 92.6% and 86.5% respectively.
- ❖ The limitation in our study could be that there was an inconsistent number of participants that were sent to colposcopy and that did an HPV E6/E7 mRNA test, therefore some participant that did an HPV E6/E7 mRNA they were not referred to colposcopy and the sample size also could have an effect in the statistical insignificance.
- ❖ It was further concluded that in further studies to understand the effect of HPV E6/E7 mRNA on cervical neoplasia a higher sample size of HR-HPV positive participant must be recruited and both tests must be done to all participants, a more controlled study.