Cervical Cancer Screening

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1st Quarter 2022

Cervical cancer is caused by chronic infection with one of 14 high-risk human papillomaviruses (HR-HPV). The risk-factor for development of cervical cancer is thus clearly defined. Most infected women will clear HR-HPV through natural immunity (usually within 2 years of acquisition), but a proportion (± 10%) will have infection that persists, resulting in cellular changes that may progress from pre-malignant dysplasia to high-grade dysplasia (CIN2, CIN3), and eventually to invasive cervical carcinoma. The timeline from exposure to the development of invasive carcinoma in the persistently infected, undetected woman is 10 – 15 years, though this may be shortened by concurrent HIV infection.

Why women should be encouraged to screen for Cervical Cancer risk?

South Africa has a population of 21.3 million women over the age of 15 years who are at risk of developing cervical cancer. Sexually transmitted infection with HPV is very common, with most women being exposed to HPV at some point in their lifetime. It is estimated that every year 10 702 South African women are diagnosed with cervical cancer and 5 870 die from this preventable disease. It is the second most frequent cancer amongst South African woman and the most frequent in women aged 15 – 44 years. HPV-16 and -18 are responsible for 64.2% of invasive cervical cancer cases. Approximately 7.9% of women are estimated to be infected with HPV-16 and -18 at any given time. HPV-45 is the third most common type associated with cervical cancer.

In addition, South Africa has a very high prevalence of HIV infection, a known risk factor for the development of cervical cancer. It is estimated that 25.8% of South African females 15 – 49 years old are infected with HIV.

With appropriate screening, cervical cancer can be prevented, by detecting cancer risk and pre-cancerous lesions, or cured, by detecting cancer early and managing appropriately. Cervical cancer is one of the only cancers that can be prevented through immunisation prior to HR-HPV exposure, or appropriate screening with readily available tests and minimally invasive procedures.

What is the most appropriate strategy for cervical cancer screening?

A screening strategy should focus on detecting women who are at risk for cervical cancer, i.e. have a persistent infection with HR-HPV, and appropriately staging her along the continuum of disease progression by means of cytology in order to select appropriate management.

Screening with cytology (Pap smear) does significantly reduce the incidence of cervical cancer, but it has a number of limitations:

- It is subjective.
- It has relatively low sensitivity for high-grade dysplasia and invasive cancer (≥ CIN2). In the ATHENA study, 1/3 of women who developed cancer had a normal Pap smear.
- It is associated with complex diagnostic categories and management algorithms.
- It identifies women who already have dysplasia rather than identifying those at greatest risk for developing high-grade dysplasia before it develops.
- HPV-18 and -45 are more common in cases of adenocarcinoma than in cases of squamous cell carcinoma. Adenocarcinomas may be missed on cytology as they are often higher up in the endocervical canal.

There is growing consensus that cervical cancer screening needs to move away from cytology as a first-line screening test.

Several large clinical trials have clearly shown that:

- Screening for the presence of HR-HPV is more sensitive than cytology for the detection of women with ≥ CIN3.
- Women identified as being infected with HR-HPV are less likely to progress to ≥ CIN3 because they receive appropriate intervention.
- The absence of HR-HPV has an excellent negative predictive value compared to cytology, allowing for longer screening intervals of 3 – 5 years.

The ATHENA study was a multicentre, prospective study conducted to evaluate screening for cervical cancer by means of HR-HPV detection, and led to the following recommendations being made with regards to cervical cancer screening:

- HPV genotyping should be used to screen women ≥ 25 years old.
- Infection with HPV-16 or -18 should be specified. This helps to triage women at highest risk, while reducing unnecessary interventions in women with transient infections due to other HR-HPV types.
- Women infected with HPV-16 or -18 should be referred for colposcopy.
- Cytology should be used to triage women infected with HR-HPV other than HPV-16 or -18. Women with abnormal cytology should be referred for colposcopy.

Sexually active women < 25 years old should be screened with cytology. This is to avoid over-investigation of transient HR-HPV infections that would be detected with HPV screening.

Self-sampling

Data from the private and public health sector indicates that the vast majority of South African women do not screen for cervical cancer. There are many reasons for this including cost, time and reluctance to have a cervical sample collected. Self-sampling has been shown to be reliable for HPV testing and has been rolled out in a number of countries as part of their cervical cancer screening programmes, including the Netherlands, Australia, and the UK. This allows a woman to collect her own sample, at a time and location convenient for her. Based on the HPV result obtained, she can then be directed to consult with a gynaecologist or general practitioner, or repeat screening after an appropriate timeframe. The Department of Health recognises self-collection as an acceptable and effective modality for increasing access to cervical cancer screening.

Self-sampling for HPV testing is not recommended:

- Under the age of 25 years;
- If the woman is pregnant;
- If the woman is symptomatic with abnormal vaginal bleeding, pain or discharge;
- If woman has had a total hysterectomy because of pre-cancerous or cancerous changes in the cervix

In these settings the women should have a healthcare worker collected sample.

A liquid-based cytology sample collected by a healthcare worker (HCW) is still considered the sample of choice as it can be used for both cytology and HPV testing. The interaction with the HCW also provides an opportunity for the woman to be examined for other conditions. However, with so many women not presenting to a HCW, self-collection will increase the number of women screening, and help prevent unnecessary cervical cancer cases and deaths.

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