HPV the silent killer, Prevention and diagnosis

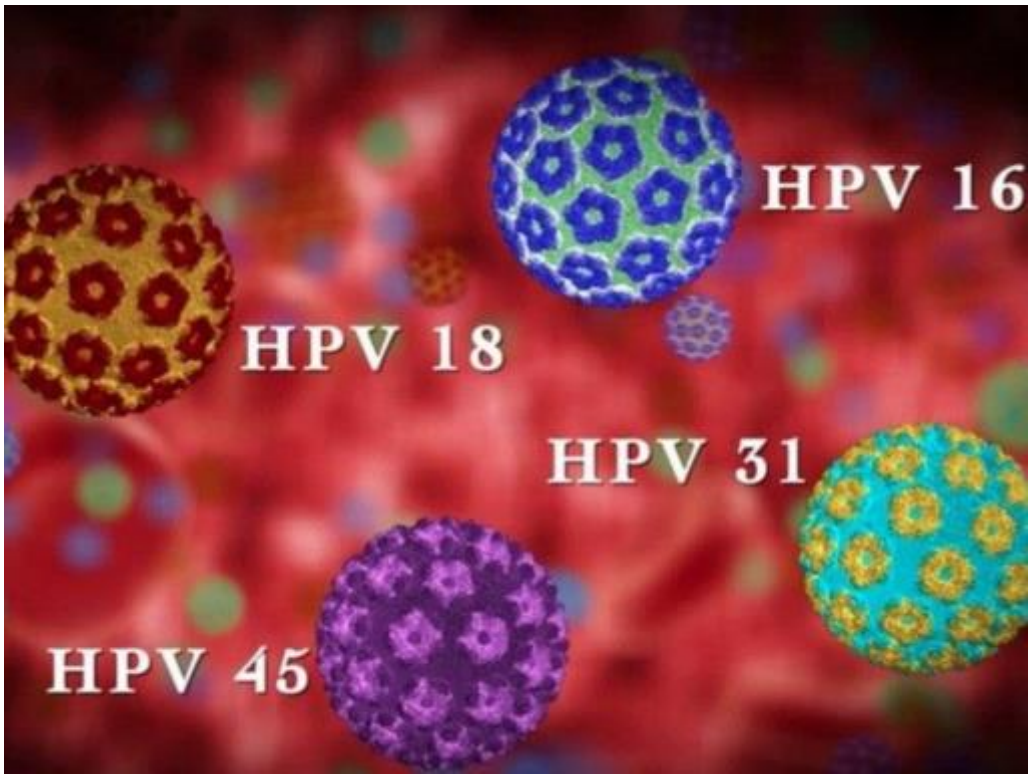
HPV

Human Papilloma Virus is a name given for a silent virus transmitted sexually most of the time, a virus that spreads in the name of love, passion, and sex.

Once a person contracts it, the journey begins with mixed and turbulent emotions that will accompany the patient through all the steps from diagnosis to treatment.

In the Middle East this topic is neglected and rightfully so under diagnosed.

We will discuss the virus, its behavior, the impact on health, the diagnosis and prevention as well as treatments.



What is the natural history of HPV?

Human papillomavirus is divided into two classes: 1) oncogenic and 2) nononcogenic. Infection with oncogenic (or high-risk) HPV usually is a necessary but not sufficient factor for the development of squamous cervical neoplasia. Therefore, only a small fraction of women infected with high-risk HPV will develop significant cervical abnormalities and cancer. The current model of cervical carcinogenesis posits that HPV infection results in either transient or persistent infection.
Most HPV infection is transient and poses little risk of progression. Only a small fraction of infections are persistent, but persistent infection at 1 year and 2 years after initial infection strongly predicts subsequent risk of cervical intraepithelial neoplasia (CIN) 3 or cancer regardless of age.

Factors that determine which HPV infections will persist are incompletely understood. The HPV genotype appears to be the most important determinant of persistence and progression. Human papillomavirus-16 has the highest carcinogenic potential and accounts for approximately 55–60% of all cases of cervical cancer worldwide. Human papillomavirus-18 is the next most carcinogenic genotype and is responsible for 10–15% of cases of cervical cancer.

When should screening begin?

Cervical cancer screening should begin at age 21 years. With the exception of women who are infected with HIV or who are otherwise immunocompromised, women
younger than 21 years should not be screened regardless of the age of sexual initiation or the presence of other behavior-related risk factors (Table 1). The recommendation to start screening at age 21 years regardless of the age of onset of sexual intercourse is based on the very low incidence of cancer and the lack of data that screening is effective in this age group. Only 0.1% of cases of cervical cancer occur before age 20 years, which translates to approximately 1–2 cases per year per 1,000,000 females aged 15–19 years. Further, studies from the United States and the United Kingdom have demonstrated that screening younger women has not decreased their rate of cervical cancer.

Human papillomavirus infection is commonly acquired by young women shortly after the initiation of vaginal intercourse and other sexual activity. Nearly all cases are cleared by the immune system within 1–2 years without producing neoplastic changes. Although cancer is rare in adolescents, neoplasia is not. In a report of 10,090 Pap test results in females aged 12–18 years, 422 specimens (5.7%) were reported as LSIL and only 55 specimens (0.7%) were HSIL.

Earlier onset of screening than recommended may increase anxiety, morbidity, and expense and lead to overuse of follow-up procedures. The emotional effect of labeling an adolescent with a sexually transmitted infection and potential precancer must be considered because adolescence is a time of heightened concern for self-image and emerging sexuality. Studies have documented a significant increase in rates of preterm birth among women previously treated with excisional procedures for neoplasia.

Table 1. Screening Methods for Cervical Cancer for the General Population: Joint Recommendations of the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology

Population

Women younger than 21 years

No screening

Women aged 21–29 years

Cytology alone every 3 years

Women aged 30–65 years

Human papillomavirus and cytology cotesting (preferred) every 5 years Cytology alone (acceptable) every 3 years

Screening by HPV testing alone is not recommended*

Women older than 65 years

No screening is necessary after adequate negative prior screening results

Women with a history of CIN 2, CIN 3, or adenocarcinoma in situ should continue routine age-based screening for a total of 20 years after spontaneous regression or appropriate management of CIN 2, CIN 3, or adenocarcinoma in situ.

Women who underwent total hysterectomy

No screening is necessary

Applies to women without a cervix and without a history of CIN 2, CIN 3, adenocarcinoma in situ, or cancer in the past 20 years

Women vaccinated against HPV

Follow age-specific recommendations (same as unvaccinated women)

How do we prevent and minimize the transmission of HPV?

VACCINATION

Human Papillomavirus Vaccines

The U.S. Food and Drug Administration (FDA) has approved three vaccines that are effective at preventing HPV infection. These vaccines cover 2, 4, or 9 HPV serotypes, respectively. The HPV vaccine is recommended for girls and boys aged 11–12 years and can be given to females and males up to age 26 years. For girls and boys who receive their first dose of HPV vaccine before 15 years of age, only two doses are needed. The timing of the two doses is 0 (baseline) and 6–12 months. If the interval between the two doses is less than 5 months, a third dose is recommended . An interval greater than 12 months is not recommended in order to ensure both doses are given before the onset of sexual activity. If females or males receive their first dose at 15 years of age or older, three doses are needed and given at 0 (baseline), 1–2 months after the first dose, and 6 months after the first dose.

The durability of the immune response (ie, how long protection lasts) is being monitored in long-term studies, and currently there is no indication for a booster vaccine. The vaccine series does not need to be restarted in the case of a delay in administration of the second or third dose.

Although obstetrician–gynecologists are not likely to care for many patients in the initial HPV vaccination target group, they have the opportunity to educate women about the importance of vaccinating their children at the recommended age. Obstetriciangynecologists and other health care providers play a significant role and should educate parents in their decision making regarding vaccinations for male and female children.

How safe is the vaccine?

Safety data for all three HPV vaccines are reassuring. According to the Vaccine Adverse Events Reporting System, more than 60 million doses of HPV vaccine have been distributed since 2006, and there are no data to suggest that there are any severe adverse effects or adverse reactions linked to vaccination. The 9-valent and quadrivalent vaccines had similar safety profiles, except that the 9-valent HPV vaccine had a higher rate of injection site swelling and erythema than the quadrivalent HPV vaccine, and the rate increased after each successive dose of the 9-valent HPV vaccine. Obstetriciangynecologists and other health care providers should counsel patients to expect mild local discomfort after the vaccination and that such discomfort is not a cause for concern. Available data demonstrate no safety concerns in individuals who were vaccinated with the 9-valent HPV vaccine after having been vaccinated with the quadrivalent HPV vaccine.

Human Papilloma Virus and cervical cancer in the Arab World

HPV prevalence in the Middle East

HPV related infections are less common in the Middle East region compared with the rest of the world, though the exact prevalence of HPV is not as well determined as it is for other countries. In recent years, several studies have attempted to study the prevalence of HPV in the general population in the Middle East region.

The Executive Board of the Health Ministers' Council for GCC States published a report in 2005 "1998–2005 Cancer Incidence Report of Gulf Corporation Council States", which states that cervical cancer is the 11th most common cancer in the GCC states. The report further shows that between January 1998 and December 2005, there were 1,314 cervical cancer cases reported from all GCC states, accounting for 1.8% of all cancers and 3.6% of cancers among females. The overall rate for women in all GCC States was 3.0 per 100,000 of the population. Qatar reported the highest incidence of cervical cancer (8.4 per 100,000 women) followed by Oman (7.8), Bahrain (6.5), UAE (5.9), Kuwait (4.5), and KSA (2.2). The UAE's Cancer Registry Program revealed that the annual average of the reported cervical cancer cases had tripled in 2005 when compared with that from 1998-2004. However, this report only determined prevalence up to 2005 and only in the GCC states.

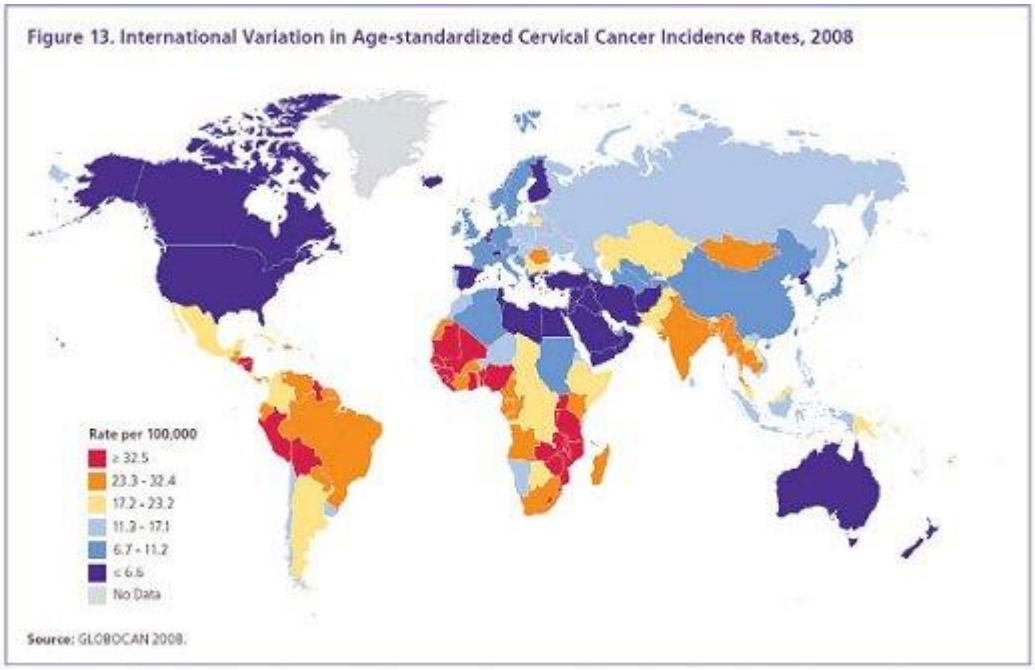


FIGURE 1: International variation in age standardised cervical cancer incidence rate, Globocan 2008

Globocan 2008 estimated incidence rate of cervical cancer among women in the Middle East, up to 2008, to be ~6.6 per 100,000 (Figure 1). This incident rises in the UAE to 6.7-11.2 per 100,000. The overall incident in the Middle East region had increased from the previous Globocan 2002 figure of 4.3 per 100,000 and had almost doubled from the GCC Report published in 2005.

Another study presented at the American Society of Clinical Oncology (ASCO) 2010 meeting by MA Seoud and colleagues utilised a large literature survey to specifically determine HPV prevalence, rather than just cervical cancer prevalence, in the Middle East & North Africa (MENA) region. The study determined, using data available from literature published up to 2009, that the prevalence of HPV is around 5%-12% in the general population and 60%-90% of cervical cancers in the MENA region are positive for HPV with HPV 16 as the most predominant type.

Further to the literature review carried out by Seoud et al in 2009, recent studies have also been performed to look at the prevalence of HPV in the Middle East. A recent study published by A Al-Thani and colleagues in Qatar examined the prevalence of different HPV types in 95 women living in Qatar. The results showed a prevalence of up to 70% of high-risk HPV types in women with gynecological problems. However, it must be emphasised that this study was carried out in women with pre-existing gynecological problems and the results do not represent the general population of Qatar.

Another recent study presented at The International Human Papillomavirus Conference and Clinical Workshop in July 2010 by S Akhtar of Kuwait University, reported a systematic review carried out to assess the prevalence of genital HPV infection in women of the Middle East. The results of the review suggest that the prevalence of HPV infection ranged from 5% to 31% in the general population, 80% among women with cytological abnormalities and almost 100% among women with cervical carcinoma. Specific prevalence of HPV infection ranged from 4.9% in

Lebanon, 13% in Palestine, and 31.6% in Saudi Arabia. Women with cytological abnormalities had much a higher prevalence of about 80% in Turkey and Saudi Arabia, where it was almost 100% among women with cervical carcinoma. The predominant HPV subtypes were HPV-16/18.

More recent studies in specific countries, published between 2010 and 2011, include a study of 3,011 Kuwaiti women, by Al- Awadhi R et al, showing that 40.8% of all HPVs were found in women 30-39 years of age, 29.6% in women 40-49 years of age, 19.7% in women over 50 years and 9.9% in women less than 34 years old. The prevalence of positive HPV findings of 5.5% was also shown in a cohort of 402 females in Iran.

Specific data is not yet available on the HPV burden in the general population of United Arab Emirates. However, a 2010 World Health Organisation (WHO) paper (United Arab Emirates: Human Papillomavirus and Related Cancers, Fact Sheet 2010), reported that every year an estimated 48 women are diagnosed with cervical cancer and 2 die from the disease (an incidence rate of 9.9 per 100,000 women). Cervical cancer ranks as the 4th most frequent cancer among women in United Arab Emirates, and the 3rd most frequent cancer among women between 15 and 44 years of age.

Traditionally the Middle East and north Africa region has been protected somewhat from HPV infections because of more conservative sexual behavior in this region. However, lately an unexpected increase of HPV infections in women in the Middle East and north Africa region has occurred because of an increase in individuals aged 10–24 years engaging in premarital sexual activity. This, coupled with the fact that the introduction of HPV vaccines has been slow because of religious and cultural sensitivities governing sexuality, financial constraints, weak infrastructure, political instability, and competition with high priority vaccines in the Middle East and north Africa region, means that an increase in HPV infection cases seems to be a recipe for disaster.

Since invasive cervical cancer cases are low in the Middle East and north Africa, no organised screening system exists, so cervical cancer is usually diagnosed in advanced stages. Additionally, only a few studies have been done on the prevalence of HPV infection in the Middle East and north Africa region. Therefore, the cost-effectiveness of vaccines is difficult to judge because the Middle East and north Africa countries do not have interpretive technical capacities.