

Cervical Cancer Prevention in Saudi Arabia: It is Time to Call for Action!

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Abstract: *Background:* Cervical cancer is the third most common cancer in the world, with 2.3 million prevalent cases and 510,000 incident cases documented each year. Annually, 288,000 women die of cervical cancer, and 80% of these deaths occur in developing countries. The population of Saudi Arabia is young and growing at an increasing rate. The estimated number of new cases of cervical cancer in 2025 is 309. Lack of comprehensive information on cytological cervical abnormalities and cervical Human Papilloma virus (HPV) infection in Saudi Arabia.

Objectives: One aim of this review is to understand the current status of cervical cancer in Saudi Arabia. Based on this information, another aim is to formulate recommendations for cervical cancer prevention that can be applied in our local setting.

Methods: An English literature search was conducted using the Pub Med data base between January 2000 till June 2011, which aimed to review all the publication which was done regarding cancer cervix and cervical dysplasia in the kingdom of Saudi Arabia.

Suggestions and Recommendations: Screening should be started at a later age and should include human papillomavirus (HPV) testing. The age of onset of screening should be determined based on data collected regarding the age of sexual debut for women.

Keywords: Saudi Arabia, cervical cancer, prevention.

BACKGROUND

Saudi Arabia is a Muslim country with an estimated population of 25 million. Approximately 7 million individuals in the population are non Saudi, with 2 million of them being women. The population is young and growing at an increasing rate (Table 1) [1]. Cervical cancer is the third most common cancer in the world, with 2.3 million prevalent cases and 510,000 incident cases documented each year [2, 3]. Annually, 288,000 women die of cervical cancer, and 80% of these deaths occur in developing countries [3]. This is particularly disturbing, because cervical cancer is a preventable disease. It is anticipated that as the population ages, there will be a dramatic increase in the incidence of cervical cancer [2].

Pap smear screening, which identifies cytological abnormalities of the cervical transformation zone, has helped to reduce cervical cancer incidence and mortality rates by 70% in developed countries [4]. The incidence of cervical cancer is low in Saudi women. According to the Saudi registry 2007 report, cervical cancer is the 13th most frequent cancer in Saudi women and the 6th most frequent cancer in Saudi

women between 15 and 44 years of age [5]. This is in contrast to Canada where it is the second most common cancer in this age group [6]. The incidence rate in Saudi Arabia is one of the lowest in the world at 1.9 cases per 100,000 women, accounting for 2.6% of diagnosed cancer cases in women. In Canada, where they have active screening, the most recent cervical cancer rate is 7 cases per 100,000 women and the most recent mortality rate is 3 deaths per 100,000 women [6]. Prior to the introduction of screening, the rates were greater than 25 cases per 100,000 women, which is comparable to current rates in many nations in Central America [7].

Current estimates in Saudi Arabia indicate that every year, 152 women are diagnosed with cervical cancer and 55 die from the disease. It is anticipated that as the population ages, there will be a dramatic increase in the incidence of cervical cancer. The estimated number of new cervical cancer cases and deaths in 2025 are 309 and 117, respectively [1]. The aim of this review is to understand the current status of cervical cancer in Saudi Arabia. Based on this information, another aim is to formulate recommendations for cervical cancer prevention that can be applied in our local setting.

Methods. A search was conducted by Two Gynecological oncologist practicing in Saudi Arabia and was verified by two Canadian consultants in the same specialty. An English literature search was conducted using the Pub Med data base between January 2000 till June 2011, which aimed to review

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Table 1. Female Saudi Arabia Population According to Age from 2000-2010

Age (year)	2000	2005	2010
15-19	1.05	1.3	1.5
20-24	0.7	1.1	1.3
25-29	0.55	0.7	1.1
30-34	0.5	0.6	0.8
35-39	0.5	0.51	0.7
40-44	0.4	0.5	0.6

Reference: http://www.nationmaster.com/country/sa-saudi-arabia/Age_distribution.

all the publication which was done regarding cancer cervix and cervical dysplasia in the kingdom of Saudi Arabia. Additional references were used to cover some of the literature about cervical cancer prevention in Muslim countries.

RESULT

In Saudi Arabia, most centre using conventional cytology for opportunistic screening for cervical cancer. Recently, some centre adopted the used of liquid based cytology as a methods of screening which help to do HPV testing . There is limited hospital – based data regarding pap smear abnormalities (Table 2) [8-12].

Cervical cancer is caused by sexual exposure to an oncogenic type of the human papillomavirus (HPV), usually types 16 and 18 [13-16]. Currently, little is known about the prevalence on HPV in Saudi Arabia. In a study performed in 120 Saudi and other Arab women undergoing a routine gynecological examination, Al-Muammar *et al.* found the overall prevalence of HPV-16/18 was 31.6%. The prevalence of HPV-16 and HPV-18 alone were 13.3% and 3.3%, respec-

tively. The prevalence of HPV-16 as a mixed infection with HPV-18 was 15% [17]. In contrast to this high prevalence, another study was conducted in the western region of Saudi Arabia by Gazaz of one hundred women were enrolled in this study. HPV DNA testing by HC2. They were 5 (5%) high-risk HPV, one low-risk HPV (1%) [18].

The distribution of HPV subtype in cancer cervix in Saudi Arabia still not been extensively studied. On one of the study of a hundred patients with cervical cancer in Saudi population they reviewed, 89% were HPV-positive. The most common HPV genotypes were 16 (65.2%), 31 (7.9%), 45 (6.7%), 18 (3.4%), and 73 (2.3%) [19]. However, these results seem to be different from those obtained in another Middle Eastern country where the most common HPV genotype was 33 followed by 16 and 18 [20]. Another study which conducted by Sait *et al.*, of 38 patients with cervical dysplasia and invasive disease. HC2 testing for high risk HPV were found to be positive in patients with cervical dysplasia, invasive carcinoma and all in 5 (29.4%) ,13 (61.9%) and 18 (47.4%) , respectively [21].

Table 2. Summary of Reported Data on Pap Smear Abnormalities in Saudi Arabia

Author ^a	Duration	Total no	Abnormal PAP smear	ASC-US	ASC-H	LSIL	HSIL	AGUS	Invasive Cancer
Al-Jaroudi (8)	2008-2009	241	7 (2.9%)	3 (1.2%)	1 (0.4%)	2 (0.83%)	NR	1 (0.4%)	NR
Jamal (9)	1984-2000	22089	368 (1.66%)	88 (0.4%)	NR	81 (0.37%)	72 (0.32%)	36 (0.16%)	26 (0.1%)
Altaf (10)	2001	3088	97 (3.14%)	14 (0.45%)	NR	29 (0.93%)	17 (0.55%)	4 (0.13%)	5 (0.16%)
Abdullah L (11)	1998 - 2005	5590	261 (4.7%)	103 (1.84%)	6 (0.10%)	5 (0.09%)	31 (0.55%)	30 (0.53%)	2 (0.04%)
Altaf (12)	2000-2004	5132	241 (4.7%)	124 (2.4%)	NR	31 (0.6%)	22 (0.4%)	58 (1.1%)	6 (0.1%)
Total		36140	974 (2.6%)	306 (0.8%)	7 (0.02%)	131 (0.36%)	119 (0.33%)	181 (0.5%)	56 (0.15%)

^aReferences: [8-12].

ASC-US: atypical squamous cells of undetermined significance; ASC-H: atypical squamous cells, cannot rule out high-grade lesion; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; AGUS: atypical glandular cells of undetermined significance; NR: not reported.

The total number of patients who had a PAP smear was 36,140, with an overall rate of abnormal PAP smears of 2.6%. The society and standards of mores could make Muslim women less susceptible to HPV infection [18, 22].

Although cervical cancer is both preventable and curable, most women in Saudi Arabia present at advanced stages [23, 24] that require extensive chemo-radiation therapy. This is due to the lack of a proper screening program [25].

Improvement in cervical cancer prevention is provided by HPV screening and vaccination, which is an effective measure for many infectious diseases [26]. Natural HPV infections are inefficient in eliciting a protective immune response [27]. Vaccines have been developed against HPV infection to prevent cervical cancer and other HPV-related diseases [28]. Two vaccine types, a bivalent (Cervarix) vaccine that protects against HPV-16 and -18 and a quadrivalent (Gardasil) vaccine that is effective against HPV-6, -11, -16 and -18, are being widely introduced in Western countries [28, 29].

Exposure to HPV can be minimized by the vaccination of young women. Vaccination is most effective when applied to young women before they become sexually active (primary prevention). Precancerous cellular changes can be identified through screening, assessment of test-positive cases, and treatment (secondary prevention). The goal of secondary prevention is to prevent cancer; however, it may also identify cervical cancer at an earlier stage, which will increase the likelihood that treatment will be successful. Secondary prevention for cervical cancer involves identifying women with cervical intraepithelial neoplasia [3, 30] and treating it to prevent the occurrence of cancer.

Currently available tests include cytologic evaluation, visual tests, and tests for HPV infection. There are several recognized obstacles to cytology-based screening, including the need for required laboratory infrastructure, trained specialists for processing and reporting, quality control, and a system of communication to the women screened so that they may receive sufficient treatment. The necessity for multiple visits with cytology-based screening results in significant loss to follow-up [15, 16]. Visual inspection after the application of 3% to 5% acetic acid (VIA) [31-33] and HPV testing identify a reproducible profile of women who are at high risk of developing precancerous or cancerous lesions [34-36]. When used alone, or in combination with VIA, HPV DNA testing has shown great promise [37, 38].

In this part of the world, there should be some concern regarding the quality assurance of cytology findings given the low prevalence of disease. Colposcopy services for the triage of patients with abnormal screening examinations are not widely available. Although gynecologic oncology services are realistically just being developed, they do exist in major centers and have well-trained physicians capable of treating women with invasive disease. Similarly, facilities for radiation oncology have been established.

FORESEEABLE CHALLENGES

1. To understand the prevalence of high-risk (HR)-HPV infections and the prevalence of abnormal cytology findings in general population.

2. To understand the sexual practices of the population.
 - a. By region and population group.
3. Implementation of any screening program, either primary or secondary, will be difficult in patients with a sexually transmitted infection.
4. Vaccination – is it cost-effective given the low rates of cervical cancer?
5. Introduction of quality assurance in screening and colposcopy.
6. Which screening method should be used and how does one triage the patients?

SUGGESTIONS:

1. Basic research:
 - a. We need to know the prevalence of HR-HPV and which genotypes are present.
 - i. Regional survey (not just based at one hospital).
 - ii. Confidential swab of the cervix obtained at a set time for HPV testing, with PCR testing and the possibly of doing cytologic evaluation if positive.
 1. Would an antenatal clinic present an opportunity for such testing?
 2. Is there any other time when performing a vaginal examination or testing is acceptable?
 3. Could one do self-collection with a vaginal swab?
 4. We need to look into the acceptability of this.
2. We need to understand the age of sexual debut. Is it similar to the age of marriage? We need to evaluate the age distribution of the women with cervical cancer. This is to ensure that the screening done is not started too early, leading to the possibility of overtreatment.
3. The HPV vaccine is an ideal solution, but it is not likely to be cost effective for all women. Screening with cytology has a low sensitivity (55%) in North America, where there is a high prevalence of abnormal screening tests [39]. In Saudi Arabia, this sensitivity would be further decreased due to a lower incidence of abnormalities. Other options, including VIA triage, are unlikely to be helpful given the low incidence of dysplasia.
4. Evaluation of the acceptability of self collection of HPV-testing.

RECOMMENDATIONS FOR PREVENTION OF CANCER OF THE CERVIX IN SAUDI ARABIA

Thus, we would suggest starting screening at a later age and with HPV testing. The age of onset should be determined based on data collected regarding the age of sexual debut for women. Screening could start as late as 25-30 years, unless many of the identified cancers have occurred in this age group. The secondary testing could be with cytology or move directly to colposcopy in women older than 35 years of age. A recent study from Italy used this algorithm, and the referral rate for colposcopy was 3-4 times higher in the HPV-positive group [40]. Screening could be done every 5

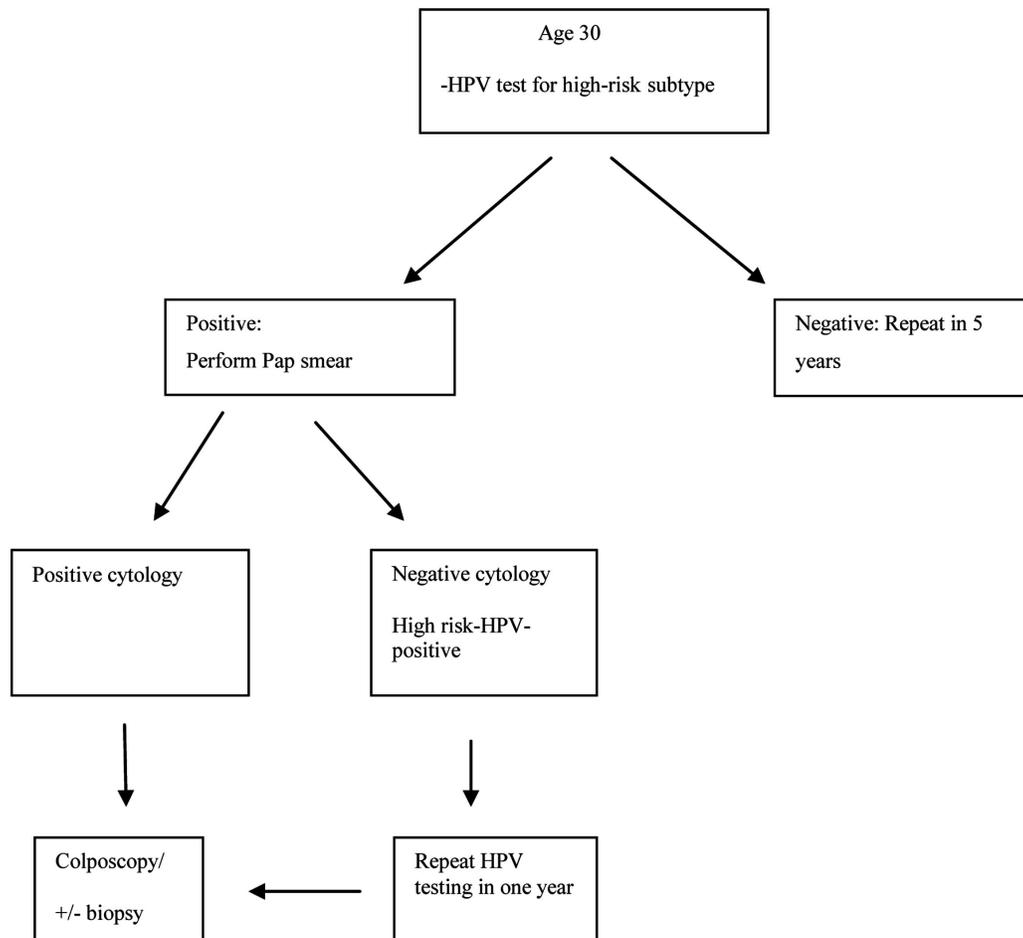


Fig. (1). Recommendations for screening program for cervical cancer in Saudi Arabia.

years with an HPV test (Fig. 1). The evidence would suggest that there is a very low incidence of cervical cancer for up to 8 years following a negative HPV test. Standard colposcopy guidelines are available in other countries, and we anticipate that the Canadian guidelines will soon be approved for publication and can be used as a guide for treatment in Saudi Arabia as well.

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CONFLICT OF INTEREST

None Declared.

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