

# High-risk human papillomavirus infection among women with pap smear tests negative for intraepithelial lesions or malignancy

## Abstract

Cervical cancer is one of the most common cancers in United Arab Emirates (UAE) as well as in the world; high-risk human papillomavirus (HR-HPV) infection is found to be the most common cause of cervical cancer. The objective of the study is to evaluate the status of HR-HPV infection among women with Pap smear tests negative for intraepithelial lesions/malignancy (NILM). This cross-sectional study was conducted at the GMC Hospital and Gulf Medical University Histopathology/Cytology and Molecular Biology Laboratories within a period of 6 months from December 2011-May 2012. All pertinent patients' data were obtained from medical records. A total of 50 patients were included in the study. Cytology (PreservCyt) samples were tested for HR-HPV, using the polymerase chain reaction (PCR) based test AMPLICOR HPV. This test is designed to detect 13 HR-HPV type. Data was analyzed using the Statistical Package for Social Sciences (SPSS) software package and was presented mainly as percentages of total sample size. **Results:** Of the 50 patients, five (10%) were positive for HR-HPV. Only four patients out of the 50 patients (8%) underwent Pap smear test as voluntary routine check-up, while 46 patients (92%) underwent the test because they were symptomatic. **Conclusions:** We acknowledge the small size of our working sample, but in view of very limited data in the region and due to strong cultural taboos against the topic, we have drawn some high level statistical conclusion and found that a moderately high prevalence of HR-HPV positive patients among women with Pap smear test NILM was detected in UAE, a country where no community based cervical cancer screening program is practiced. The rate of opportunistic/voluntary cervical screening was very low indicating poor or lack of awareness about the importance of Pap smear test as a tool to screen cervical epithelial changes among study population. The results presented in this study may provide valuable data for physicians involved in decision-making regarding the current situation related to cervical screening practice and HPV infection in UAE.

**Key words:** Cervical cancer, HPV, UAE

**Nehmat El Banna,  
Ghaith Al Eyd<sup>1</sup>,  
Reem Salim Saeed<sup>2</sup>**

Departments of Molecular Biology and <sup>1</sup>Pathology, Gulf Medical University, Ajman, <sup>2</sup>Department of Microbiology, Sheikh Khalifa Hospital, Ajman, United Arab Emirates

### Address for the Correspondence:

Dr. Nehmat El Banna,  
Department of Molecular Biology,  
Gulf Medical University,  
Ajman, United Arab Emirates.  
E-mail: drnehmat@gmail.com

### Access this article online

Website: [www.ijmedph.org](http://www.ijmedph.org)

DOI: 10.4103/2230-8598.127168

Quick response code:



## INTRODUCTION

In spite of the fact that cervical cancer is considered a preventable disease it is one of the most common cancers among women worldwide. In 2008 cervical cancer was the third most common cancer in women worldwide after breast and colorectal cancer, with an estimated 529,000 new cases and 275,000 deaths, of which 88% were in developing countries. In some regions it is the number one cause of cancer-related deaths.<sup>[1]</sup>

In 2005 cervical cancer ranked sixth most common cancer in women in GCC countries, accounting for 3.6% of cancers among females. Age adjusted incidence rate in United Arab Emirates (UAE) reached 7.4 per 100,000 in 2008.<sup>[2]</sup>

Like other cancers which are mainly caused by infectious agents, such as liver cancer and stomach cancer, the disease is markedly over represented in less developed countries, constituting more than 85% of the global burden of cervical cancer.<sup>[3,4]</sup>

Cervical cancer's incidence differs largely between regions reflecting the differences in availability of preventive programs against cervical cancer, lifestyle, and the position of women in society. In

view of the wide variation of mortality, incidence ratio reflects the inequalities in accessibility of well-functioning health services delivery to ensure early detection and timely treatment of cervical precancer and cancer cases.<sup>[3,5]</sup>

A persistent oncogenic or so called high-risk human papillomavirus (HR-HPV) infection was found to be a leading cause in the development of cervical cancer.<sup>[6]</sup> Cytopathologically, the control over cell growth is disrupted by the virus and over years or even decades, will lead to asymptomatic precancerous lesions and might progress into invasive cancer.<sup>[6]</sup> Some studies have suggested the appearance of precancerous or cancerous lesions within 2 years of HPV infection at a young age group.<sup>[7,8]</sup>

Recently, with newer sophisticated techniques for HPV detection, HPV could be eventually identified in virtually all (99.7%) adequate cervical cancer samples.<sup>[1,9]</sup>

The most frequently occurring HPV types in invasive cervical cancers (ICCs) are HPV 16, 18, 58, 33, 45, 31, 52, 35, 59, 39, 51, 56, and 68. HPV 16 and/or 18 were associated with 73% of all cervical cancer cases.<sup>[10,11]</sup> This is in accordance with the HPV types defined as carcinogenic by the International Agency for Research on Cancer (IARC).<sup>[12]</sup>

HPV infection and its consequences are necessary prerequisite for almost all ICC,<sup>[9]</sup> but HPV does not cause a systemic infection and often induces no inflammatory response, thus the patient is typically asymptomatic and only 50% of HPV DNA positive patients will have a neutralizing measurable antibody response.<sup>[13]</sup>

Estimations of prevalence of genital HPV DNA ranges from 7 to 37% depending on the country and the age of the cohort for the study.<sup>[14]</sup> About 50-80% of sexually active men and women are estimated to become infected with low- or high-risk HPV sometime in their lives.<sup>[15]</sup> A prevalence estimate of the worldwide age specific HPV infection among women with normal cytology was 10.4% in 2007 with large variation between geographic areas. The lowest observed prevalence was in southeastern Asia (6.2%) and the highest in eastern Africa (31.6%).<sup>[16]</sup>

While no data is available about the prevalence of HPV among women in UAE.<sup>[2]</sup> Some studies in Riyadh (KSA) and Qatar have showed a prevalence of 31.8<sup>[17]</sup> and 64% in these two countries, respectively.<sup>[18]</sup>

Early detection of cervical cancer, which can be achieved by regular screening, offers the chance to a more effective treatment. The aim of screening program is to find cancer at an earlier stage by identifying the initial molecular and cellular changes that occur in malignant cells.<sup>[19]</sup> The initiation and sustenance of the screening programs have proved successful in substantially lowering both cervical cancer incidence and mortality in developed countries. In countries lacking the screening programs, deaths due to cervical cancer are higher compared with those having institutionalized screening programs. The difference can be attributed to the fact that HPV infected women are only diagnosed when they become symptomatic or even later at

an invasive late stage.<sup>[20]</sup> It has been estimated that without Pap tests, the number of cervical cancer cases would be 75% higher.<sup>[21]</sup>

More recently, HPV deoxyribonucleic acid (DNA) testing has been suggested as an additional test for cervical cancer screening<sup>[22]</sup> taking into consideration its potential role in three main areas: (1) Triage of cases with minor cytological abnormalities or abnormalities of undetermined significance, (2) follow-up after treatment of cervical cervical intraepithelial neoplasia (CIN) and, and (3) for primary screening as an alternative or adjunct to Pap tests.<sup>[23]</sup>

The objective of the study is to evaluate the status of HR-HPV infection among women with Pap smear tests negative for intraepithelial lesions/malignancy (NILM), and to provide guidance for developing local guidelines for cervical cancer screening.

## MATERIALS AND METHODS

The study was approved by the Gulf Medical University Ethics Committee.

The study was a cross-sectional study conducted at GMC Hospital and GMU Histo/Cytopathology and Molecular laboratories.

### Study sample

From December 2011 to April 2012, remnants of all cervical ThinPrep samples diagnosed as NILM were transferred to the Molecular Biology Laboratory at GMU, Ajman for HPV DNA detection test.

All pertinent patients' data were obtained from patients' medical records. The research instrument (questionnaire) comprised questions on sociodemographic characteristics such as age, education, occupation, nationality, as well as gynecological symptoms, age of menarche, age when first married, pregnancy, age of menopause if applicable, use of hormonal therapy or intrauterine device, and duration when applicable.

### Procedure

The PreservCyt samples were transported to the Molecular Biology where DNA extraction was performed using the MagNa Pure LC Isolation station (Roche Diagnostics-Molecular Biochemicals, Germany); 400 µl of aliquots of samples were processed using the Nucleic Acid Isolation kit (Roche Diagnostics), as recommended by the manufacturer standard operating procedures. Nucleic acid was eluted in a final volume of 100 µl; 50 µl were used later for amplification. HPV DNA amplification was carried out using the Master Mix included in the AMPLICOR HPV amplification kit by Roche Applied Biotechnology.

The Target amplified is a sequence of nucleotides within the polymorphic L1 region of HPV genome, the amplification was done using a mix of HPV primers designed to amplify HPV DNA from 13 HR-HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) An additional primer pair targets the human β-globin gene to provide a control for cell adequacy, extraction, and amplification.

Two separate microwell plates were used for detection of amplified HPV and  $\beta$ -globin.

An absorbance reading of greater than 0.2 was considered positive for the presence of HPV.

### Statistical analysis

Patients data were tabulated using excel sheets, and analyzed using PASW statistics. The data was mainly presented as percentages. Due to the small sample size, further statistical analysis and testing the association of HPV positivity with different parameters was not possible.

## RESULTS

The samples tested for HPV DNA detection belong to females between the age of 22 and 65 with a mean age of  $36.6 \pm 9.46$  years. Eighty-two percent of the patients were expatriates, and only 18% were UAE nationals.

As shown in Figure 1, out of the 50 patients sampled for the study, five (10%) had their HPV DNA detection test positive for HR-HPV. The HR-HPV positive patients could have any (one or more) of the 13 types of HR-HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68), while nine (18%) of them the result was deemed invalid “or HPV could not be detected even if presents for those patients and in order to confirm the presence or absence of HR-HPV infection the test should be repeated, this was not possible in our study due to limited budgeting. The rest of the patients (72%) had the HPV DNA detection test negative for the 13 types of HR-HPV. Three out of the five (60%) patients who tested positive for the HPV DNA detection test, belonged to the middle age group.

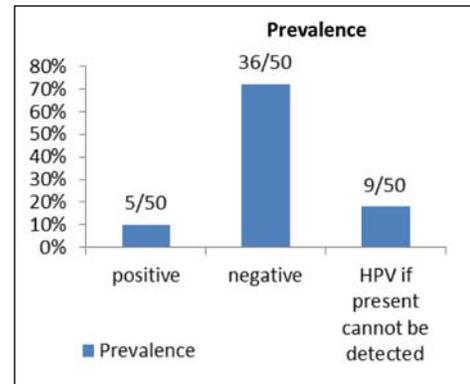
Out of the 50 patients tested for HPV DNA detection, only four (8%) underwent Pap smear testing as a voluntary routine check-up, while the 92% were symptomatic [Figure 2].

The presenting symptoms of the patients ranged from one up to three or more symptoms, more than half (52%) had vaginal discharge as the single or one of the presenting symptoms. Forty-two percent complained of an irregular bleeding, 16% had postcoital bleeding, 14% presented with pelvic pain, and 6% had postmenopausal bleeding [Figure 3].

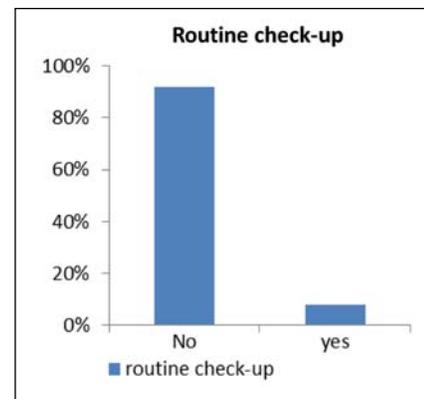
Due to the small sample size, small number of positive cases, further statistical analysis on the correlation of HPV positivity and each of the demographical characteristics was insignificant.

## DISCUSSION

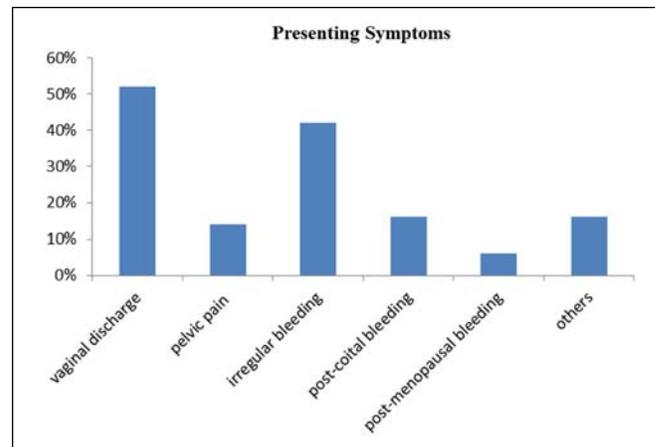
Cervical cancer is one of the most common cancers in the world and UAE. The main etiological factor for cervical cancer is HPV. After literature review and to the best of our knowledge, this is the first study concerning the status of HR-HPV in the UAE<sup>[2]</sup> and one of the very few in the region to report prevalence of HR-HPV cervical infection among women with Pap smears NILM.



**Figure 1:** Out of 50 patients, five (10%) had their HPV DNA detection test positive for HR-HPV, while for nine (18%) of them the result was invalid “or HPV could not be detected even if present”, and for 36 (72%) the test was negative



**Figure 2:** Out of the 50 patients tested for HPV DNA detection, only four (8%) underwent Pap smear testing as a voluntary routine check-up, while the 92% were symptomatic



**Figure 3:** Majority of patients (52%) presented with vaginal discharge as main symptom, other symptoms included pelvic pain, irregular, postcoital, or postmenopausal bleeding

It is crucial to determine the prevalence of an important infection such as HPV that can remain silent for years and will not become symptomatic until a serious lesion has developed. This fact necessitates the need for cervical screening for early detection of

HPV infection. Organized cervical screening is not practiced in UAE and voluntary or opportunistic screening is not culturally the norm. This is demonstrated by the fact that only 8% of the patients of this study voluntarily underwent the Pap smear test as a routine check-up, while the majority of patients (92%) presented to the gynecologist only because of their symptoms. By considering this fact; patients having Pap smear test NILM and at the same time having positive test for HR-HPV would be at a high risk of having serious HPV induced lesions in the future. These patients, after being reassured by the negative Pap smear test result, will seek a medical checkup only when they have symptoms again. By that time, HPV infection might have progressed through the required time period to induce the serious epithelial changes.

Few studies have addressed the prevalence of HR-HPV in women with Pap smears NILM in the region. In Saudi Arabia a study showed the HR-HPV positivity as (18/110) in the cytologically normal Pap smears. This rate was considered relatively high given the fact that in Saudi Arabia extramarital sex and multiple sexual partnerships are strictly prohibited.<sup>[17]</sup> Other studies in Middle Eastern countries reported much lower prevalence rates like 4.9% in Lebanon<sup>[24]</sup> and 2.7% in Kuwait.<sup>[25]</sup> While in South American countries, which have the highest incidence rate of cervical cancer, the prevalence reached 20.4%. A meta-analysis published in 2007 showed the highest prevalence to be in Africa at 22.1%.<sup>[16]</sup> A study in the United Kingdom by Howell-Jones in 2010 reported a prevalence of HR-HPV in women with normal smears to be of 12.2%.<sup>[26]</sup>

Therefore, in UAE efforts should be directed toward increasing the awareness about cervical screening, whether through organized nationwide program or opportunistic/voluntary screening. The importance of cervical screening by Pap smear test should be addressed to the patients as well as healthcare providers who should offer this test whenever possible. Few studies in the region have addressed this issue and showed the lack in Pap smear test practice, which is due to lack of knowledge or information about the test. A recent study in Ajman, UAE has showed that the rate of opportunistic screening does not exceed 0.4%.<sup>[27]</sup> A study in Kuwait showed that the main reason for not undergoing the Pap smear test was that the test was not suggested by the doctor.<sup>[28]</sup> In Qatar, 60% of patients who did not have their Pap smear tests done, would have considered the test if they have been well-informed how simple and painless this test is.<sup>[29]</sup> A similar study has been done among primary healthcare providers in the UAE reported that only (40%) of female primary healthcare providers have performed a Pap smear test once, and the majority had the desire to know more about the test performance and importance.<sup>[30]</sup>

Considering the low rate of opportunistic cervical screening in UAE and the region, educational and awareness programs about the importance of Pap smear testing for healthcare providers as well as patients, remains the best choice to enhance the early detection of any positive HPV induced epithelial abnormalities.

Among parameters which have been considered in our study are: Age, age when first married, smoking, and use of oral contraceptives. Testing the association of these parameters with the HR-HPV positivity was not possible due to the small sample size. The prevalence of HPV infection noted in some of the studies in women with negative cytology was highest among women younger than 25 years,<sup>[31,32]</sup> with a declining rate until the age of menopause where the positivity will rise again giving the pattern of U-shaped graph. A second pattern is observed in certain communities, where the HPV infection prevalence peaks in women at young age group then subsequently decline with age without a second peak at postmenopausal age.<sup>[33]</sup>

In studies conducted mainly in developing countries the prevalence of HPV infection does not decline with increasing age and the percentage of positivity is highest among middle-aged women.<sup>[34]</sup> In our study no pattern can be concluded with the small sample size, but a higher prevalence is noted in middle-aged women.

In UAE's culture, the premarital sex is rare and it is even forbidden by the law.<sup>[35]</sup> In our study, the highest prevalence of HR-HPV infection was found in women who had first married at a young age between 15 and 19 years. It is likely that at this age group the immature mucosal immune system will give a higher chance for HPV infection to occur. The association of "having the first sexual intercourse" at an early age with an increased risk of HPV infection was reported in some studies,<sup>[36]</sup> while other studies showed this association to be insignificant.<sup>[37]</sup>

## CONCLUSION

A moderately high prevalence (10%) of HR-HPV positive patients among women with Pap smear test NILM was detected in UAE where no organized cervical screening is practiced. The rate of opportunistic/voluntary cervical screening was very low (8%) indicating a poor awareness about the importance of Pap smear test, as a tool to screen cervical epithelial changes, among study population.

The results presented in this study may provide valuable data for physicians. It provides guidance for developing local guidelines for cervical cancer screening.

## Recommendations

The fact that women do not visit their gynecologists unless symptomatic and the opportunistic screening is not a norm, educational and awareness programs on cervical diseases and the importance of Pap smear test targeting both patients and healthcare providers will be the first step in enhancing the prevention of HPV induced cervical lesions.

The information available in the UAE regarding incidence of cervical cancer, epithelial cells abnormalities, and factors associated with these diseases are limited; further similar studies on a larger scale will give a clear view about the country's situation and its need for implementing preventive measures in this regard.

## REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893-917.
2. World Health Organisation. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Human Papillomavirus and Related Cancers in United Arab Emirates. Summary Report 2010. Barcelona, Spain. Available from: [www.who.int/hpvcentre](http://www.who.int/hpvcentre) [Last accessed on 2012 Jan].
3. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev* 2010;19:1893-907.
4. Cervical Cancer Statistics. Available from: <http://www.Cervical Cancer.org> [Last accessed 2012 May].
5. Sankaranarayanan R, Ferlay J. Worldwide burden of gynecological cancer: The size of the problem. *Best Pract Res Clin Obstet Gynecol* 2006;20:207-25.
6. Gustafsson L, Ponten J, Bergstrom R, Adami HO. International incidence rates on invasive cervical cancer before cytological screening. *Int J Cancer* 1997;71:159-65.
7. zur Hausen H. Papillomaviruses in the causation of human cancers — a brief historical account. *Virology* 2009;384:260-5.
8. Winer RL, Kiviat NB, Hughes JP, Adam DE, Lee SK, Kuypers JM, *et al.* Development and duration of human papillomavirus lesions, after initial infection. *J Infect Dis* 2005;191:731-8.
9. Woodman CB, Collins S, Winter H, Bailey A, Ellis J, Prior P, *et al.* Natural history of cervical human papillomavirus infection in young women: A longitudinal cohort study. *Lancet* 2001;357:1831-6.
10. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, *et al.* Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol* 1999;186:12-9.
11. Munoz N, Bosch FX, de Sanjose S, Tafari L, Izarzugaza I, Gili M, *et al.* The causal link between human papillomavirus and invasive cervical cancer: A population-based case-control study in Colombia and Spain. *Int J Cancer* 1992;52:743-9.
12. Li N, Franceschi S, Howell-Jones R, Snijders PJ, Clifford GM. Human papillomavirus type distribution in 30,848 invasive cervical cancer worldwide: Variation by geographical region, histological type and year of publication. *Int J Cancer* 2011;128:927-35.
13. Carter JJ, Koutsky LA, Hughes JP, Lee SK, Kuypers J, Kiviat N, *et al.* Comparison of human papillomavirus types 16, 18, and 6 capsid antibody responses following incident infection. *J Infect Dis* 2000;181:1911-9.
14. Bosch FX, Burchell AN, Schiffman M, Giuliano AR, de Sanjose S, Bruni L, *et al.* Epidemiology and natural history of human papillomavirus infections and typespecific implications in cervical neoplasia. *Vaccine* 2008;26 Suppl 10:K1-16.
15. Stanley M. Immune responses to human papillomavirus infection. *Vaccine* 2005; Accessed online. Available from: <http://www.sepeap.org/archivos/pdf/10041.pdf> [Last accessed on 2012 Sept].
16. de Sanjose S, Diaz M, Castellasg X, Clifford G, Bruni L, Munoz N, *et al.* Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: A meta-analysis. *Lancet Infect Dis* 2007;7:453-9.
17. Al-Muammar T, Al-Ahdal MN, Hassan A, Kessie G, Dela Cruz DM, Mohamed GE. Human papillomavirus 16/18 cervical infection among women attending a family medical clinic in Riyadh. *Ann Saudi Med* 2007;27:1-5.
18. Al-Thani A, Abu-Rub A, Al-Ansari A, Abushama M, Al-Khanji M, Al-Lawati S. Prevalence of human Papillomavirus infection in women attending gynecology /oncology clinic in Qatar. *Future Virol* 2010;5:513-9.
19. IARC. Handbooks of cancer prevention, vol. 10. cervix cancer screening. Lyon: IARC Press, 2005.
20. Liu S, Semenciw R, Probert A, Mao Y. Cervical Cancer in Canada: Changing patterns in incidence and mortality. *Int J Gynecol Cancer* 2001;11:24-31.
21. Robles SC, White F, Peruga A. Trends in cervical cancer mortality in the Americas. *Bull Pan Am Health Organ* 1996;30:290-301.
22. Petry KU, Menton S, Menton M, van Loenen-Frosch F, de Carvalho Gomes H, Holz B, *et al.* Inclusion of HPV testing in routine cervical cancer screening for women above 29 years in Germany: Results for 8466 patients. *Br J Cancer* 2003;88:1570-7.
23. Lorincz AT, Richart RM. Human papillomavirus DNA testing as an adjunct to cytology in cervical screening programs. *Arch Pathol Lab Med* 2003;127:959-68.
24. Mroueh AM, Seoud MA, Kaspar HG, Zalloua PA. Prevalence of genital human papillomavirus among Lebanese women. *Eur J Gynecol Oncol* 2002;23:429-32.
25. Al-Awadhi R, Chehadeh W, Kapila K. Prevalence of human papillomavirus among women with normal cervical cytology in Kuwait. *J Med Virol* 2011;83:453-60.
26. Howell-Jones R, Bailey A, Beddows S, Sargent A, de Silva N, Wilson G, *et al.* Study Group Collaborators. Multi-site study of HPV type-specific prevalence in women with cervical cancer, intraepithelial neoplasia and normal cytology, in England. *Br J Cancer* 2010;103:209-16.
27. Al Eyd GJ, Shaik RB. Rate of opportunistic pap smear screening and patterns of epithelial cell abnormalities in pap smears in Ajman, United Arab Emirates. *Sultan Qaboos Univ Med J* 2012;12:473-8.
28. Al Sairafi M, Mohamed FA. Knowledge, attitudes, and practice related to cervical cancer screening among Kuwait women. *Med Princ Pract* 2009;18:35-42.
29. Al-Meer FM, Aseel MT, Al-Khalaf J, Al-Kuwari MG, Ismail MF. Knowledge, attitude and practices regarding cervical cancer and screening among women visiting primary health care in Qatar. *East Mediterr Health J* 2011;17:855-61.
30. Badrinath P, Ghazal-Aswad S, Osman N, Deemas E, McIlvenny S. A study of knowledge, attitude and practice of cervical screening among female primary care physicians in the United Arab Emirates. *Health Care Women Int* 2004;25:663-70.
31. Smith JS, Melendy A, Rana RK, Pimenta JM. Age-specific prevalence of infection with human papillomavirus in females: A global review. *J Adolesc Health* 2008;43(4 Suppl):S5-25.
32. Molano M, Posso H, Weiderpass E, van den Brule AJ, Ronderos M, Franceschi S, *et al.* HPV Study Group HPV Study. Prevalence and determinants of HPV infection among Colombian women with normal cytology. *Br J Cancer* 2002;87:324-33.
33. Syrjanen K, Kumala SM, Shabalova I, Petrovichev N, Kozachenko V, Zakhrova T, *et al.* Epidemiological, clinical and viral determinants of the increased prevalence of high-risk human papillomavirus (HPV) infections in elderly women. *Eur J Gynaecol Oncol* 2008;29:114-22.
34. Li LK, Dai M, Clifford GM, Yao WQ, Arslan A, Li N, *et al.* Human papillomavirus infection in Shenyang City, People's Republic of China: A population — based study. *Br J Cancer* 2006;95:1593-7.
35. Ask the Law—Premarital sex. *Gulfnews.com*. Available from: <http://gulfnews.com/news/gulf/uae/general/ask-the-law-march-15-2002-1.381005> [Last accessed 2012 May].
36. Collinsa S, Mazloomzadeha S, Winterb H, Blomfield P, Bailey A, Young LS, *et al.* High incidence of cervical human papillomavirus infection in women during their first sexual relationship. *BJOG* 2002;109:96-8.
37. Vaccarella S, Franceschi S, Herrero R, Munoz N, Snijders PJ, Clifford GM, *et al.* IARC HPV Prevalence Surveys Study Group. Sexual behavior, condom use, and human papillomavirus: Pooled analysis of the IARC human papillomavirus prevalence surveys. *Cancer Epidemiol Biomarkers Prev* 2006;15:326-33.

**How to cite this article:** El Banna N, Al Eyd G, Saeed RS. High-risk human papillomavirus infection among women with pap smear tests negative for intraepithelial lesions or malignancy. *Int J Med Public Health* 2014;4:102-6.

**Source of Support:** Nil, **Conflict of Interest:** None declared.