

Screening of Cervical Precancerous and Cancerous lesions. A Minireview

Ahmed Mohamed Maged*Professor of Gynecology and Obstetrics Kasr Alainy Hospital, Cairo University, Cairo, Egypt*

***Corresponding Author:** Ahmed Mohamed Maged, Professor of Gynecology and Obstetrics Kasr Alainy Hospital, Cairo University, Cairo, Egypt.

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Abstract

Cancer cervix is the 4th most common malignancy among women with high prevalence highest in developing countries. Its main screening is through is the Papanicolaou (Pap) tests. However its interpretation is subjective and need women cooperation. Most cases of cancer cervix are associated with Human papilloma virus (HPV) infection. Diagnosis of HPV infection is done through clinical evaluation of any lesions, cytology or coplosopic examination. However, all these tests are subjective and may be inaccurate and serological evaluation of HPV infection is usually non reliable and cannot differentiate recent from old infections. HPV testing with simple and noninvasive method of collection is better than Pap smear for screening of cervical cancer. HPV DNA is classically detected in cervical smear and recently in urine. Urine test is easier, more accepted, easily applicable and non-invasive. There is a good agreement between positive urine test for high risk HPV DNA genotype and pathological results of cervical intraepithelial lesions.

Keywords: Screening; Cancer Cervix; HPV

Cancer cervix is reported to be the 4th most common malignancy among women [1]. Its prevalence differs among different countries being highest in developing ones (85 % of cases) [2]. The explanation behind that is related to application of the successful screening program in developed countries [3].

The main screening for cancer cervix is the Papanicolaou (Pap) tests. Its sensitivity is between 53 and 80% [4]. In developing countries, its implementation is difficult because of lack of resources, deficient covering and inadequate participation of women [5]. So searching for another test was mandatory.

Most cases of cancer cervix are associated with Human papilloma virus (HPV) infection and high risk types (16, 18, 30 and 31) are linked to precancerous and cancerous cellular changes [3].

Recently, screening of cancer cervix is more successful through HPV testing than Pap smear. HPV screening is easy, better and less invasive when compared to Pap smear [6].

Diagnosis of HPV infection is done through clinical evaluation of any lesions, cytology or coplosopic examination. However, all these tests are subjective and may be inaccurate [3].

Serological evaluation of HPV infection is usually non reliable and cannot differentiate recent from old infections [7].

Adding to these difficulties, culture of HPV is not possible and the diagnosis can be done by virus DNA directly through in situ hybridization, polymerase chain reaction, and nucleic acid amplification testing [8].

HPV testing with simple and noninvasive method of collection is better than Pap smear for screening of cervical cancer [9].

HPV DNA is classically detected in cervical smear and recently in urine. Urine test is easier, more accepted, easily applicable and non invasive [10]. The high sensitivity and specificity of urine test in detection of high risk HPV is described in a recent metaanalysis

[4]. But only few studies correlate between virus DNA in urine with the pathological precancerous cervical lesions [5,10-12].

A recent study done by Maged and his colleagues in 2018 described a good agreement between positive urine test for high risk HPV DNA genotype and pathological results of colposcopic guided punch biopsy of Cervical intraepithelial lesion (CIN) 2 and 3 [3].

A positive correlation between urine testing for high risk HPV and high grade squamous intraepithelial lesions (HSIL) was documented by other studies [13,14]. Some studies found that detection of HPV DNA in urine was lower than its detection in cervical sample (71% vs. 98%) but all the included cases had infiltrating squamous cell carcinoma [15]. In study of Sabhiyah et al, the lower detection rate of HPV DNA genotype in urine compared to cervical cytology can be explained by the presence of HSIL in 28% and ASCUS in 40% of their study population and none of ASCUS women were positive for HPV whether in cervical smear or in urine [13].

In one recent study, no positive urine test for HPV was found in women with normal Pap smear while some studies reported the presence of HPV in 15% of urine samples of patients with normal Pap smear. The explanation of that may be presence of infections outside the cervix as in the anogenital region [15].

Urine HPV DNA genotype analysis has a good predictive value for the results of the pathological lesions of the cervix so it passes the Pap smear step. Most of the previous studies predicted the presence of the high risk HPV DNA genotype in both urine and cervical swap using Cobas test or Linear Array so making the urine test reliable to detect the HPV presence not pathological effect. The urine test high sensitivity and specificity for HPV DNA genotype make it a perfect procedure of screening for cancer cervix due to high detection rate of high risk HPV types [5]. High risk HPV DNA genotype detection in urine have similar criteria of Pap smear for detection of abnormal cytology [16].

Other studies correlated the detection of high risk HPV DNA genotype in both urine and Pap smear and found a positive correlation ranged between 79% and 80% [17]. Surpan *et al* found a substantial agreement between urine test and cervical sample in detection of high risk HPV DNA using Cobas test with discordance 2 out of 24 (8.3%) [18]. Studies that correlate the detection of HPV genotype in urine and Pap smear showed discordance as HPV infected cells may exfoliate from cervix, anogenital region or urethra [17]. Using urine test for high risk HPV DNA genotype as a valid test in women with abnormal pap smear have been reported

in many previous studies [11,19]. Bernal *et al*, compared performance of Cobas test in paired urine and Pap smear and found a high rate of agreement in high risk HPV detection (88%) [19]. One population based study from rural area in India detected only 5 out of 1305 women (0.4%) positive for HPV DNA using PCR detection without including cervical HPV detection to serve as reference for HPV prevalence in population [20].

As a conclusion screening of cervical precancerous and cancerous lesion can be achieved through both Pap smear and HPV testing. There is a good agreement between positive urine test for high risk HPV DNA genotype and pathological results of CIN2 and 3.

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