

# Urethral Cytology and Penioscopy as Screening Tests for Male Consorts of Females with Human Papilloma Virus Infection

Kamal MM\*, Jaiswal SM+, Nayak SP#

## Abstract

Human Papilloma virus (HPV) infection of uterine cervix is known to be a very important risk factor for the development of cervical intraepithelial neoplasia and invasive cancer. This infection, that affects partners, is presently being investigated mostly in females. This study utilized a simple technique of urethral cytology and penioscopy to screen 38 male consorts of women with HPV infection of uterine cervix. A simple naked eye examination and examination under magnification of the male genitalia i.e. "Penioscopy" was performed. A cytologic smear was obtained from the urethra using a cytobrush. Five percent acetic acid was then applied and acetowhite areas, if any, were noted. Smears were studied for features indicative of HPV infection. 10 male consorts, all of whom were asymptomatic, showed evidence of HPV infection.

**Journal of Cytology 2007; 24 (4) : 179-182**

**Key Words :** Urethral cytology, penioscopy, HPV.

## Introduction

The venereal nature of cancer of uterine cervix has been recognized since 1842, when Rigoni Stern reported that cervical carcinoma was rare in the celibate women. The geographic clustering of cervical and penile cancer<sup>1-3</sup> and elevated rate of cervical cancer among wives of penile cancer patients<sup>4-6</sup> is indicative of the important role that the male plays in the causation of cervical cancer. Infection with Human Papilloma virus (HPV) is known to be a very important risk factor for the development of cervical intraepithelial neoplasia and invasive cancer. Although evidence of HPV infection is currently investigated only in the women, the presence of this disease that can affect partners should not be disregarded. The importance of applying 5% acetic acid to male genitalia and observing aceto white lesions, if any, by a colposcope (also called as penioscopy), in order to detect subclinical infections, has been highlighted in a number of studies.<sup>7-10</sup> Various studies have confirmed the strong relationship between presence of HPV

infection in the penis of males and the risk of cervical cancer in their wives.<sup>1-3</sup> Hence the diagnosis and therapy of HPV infection in men could lead to a decrease in the reservoir of the virus responsible for female genital neoplasia.<sup>11</sup> In view of the potential benefit that can be derived by regularly screening men for clinical and subclinical HPV infection, this study was undertaken to assess the prevalence of HPV infection utilizing a simple screening technique of urethral cytology and penioscopy.

## Materials and Methods

This cross sectional diagnostic test study included 38 male consorts of women with HPV infection of uterine cervix, diagnosed by biopsies (26 cases), cytology (6 cases) and colposcopic examination (6 cases). Women who were found positive for HPV infection were requested to visit the cervical cancer screening center with their husbands. A simple naked eye examination and examination under magnification of the male genitalia was first performed. The entire external genitalia including shaft of penis, prepuce,

\*Associate Professor, +Ex-Resident, #Lecturer; Department of Pathology, Government Medical College, Nagpur. Maharashtra.

**Received :** 20.07.2007; **Revised :** 19.09.2007; **Accepted :** 15.10.2007

**Corresponding Author:** Dr. M.M. Kamal, MA/8 Laxminagar, Nagpur-440022

**E-mail:** dr.mmkamal@gmail.com

glans, corona and urethral meatus, skin of the scrotum, anus and perineum were examined using magnifying glass with 5x to 10x magnification for the presence of any warty lesion.<sup>11</sup> For convenience both the methods of magnification were included under the term "Penioscopy" i.e. examination of penis under magnification.

After thorough inspection of the genitalia, a cytologic smear was obtained from the urethra using Acellon Combi (Multi Biosampler). The cytobrush was moistened with normal saline and advanced in the distal urethra 2 to 3 cm deep. It was then rotated half a turn in each direction and then withdrawn. The tip of the cytobrush was rolled over the glass slides that were appropriately numbered with the diamond pencil. Two wet slides were immediately fixed (within 10 seconds of their preparation) in 95% ethyl alcohol for Papanicolaou stain. Two slides were air dried and stored for Giemsa stain. After collecting the smear, 5% acetic acid was applied to whole of the external genitalia with the help of gauze pieces. After 3 minutes aceto-white lesion, if any, was noted (Fig 1).

The cytologic features followed in the present study that are indicative of HPV infection were according to the criteria mentioned in the studies of Boon et al<sup>10</sup> and Gupta et al.<sup>12</sup>

Histopathologic features for the diagnosis of HPV infection and cervical intraepithelial neoplasm (CIN) were according to the criteria given by Crum.<sup>13</sup>

### Observations

The 38 women who were positive for HPV infection belonged to the age group of 36-55 years. Of these 36 were asymptomatic while 2 had complaints of burning and increased frequency of micturition. After investigations, both patients were found to be diabetics with urinary tract infection. 10 male consorts

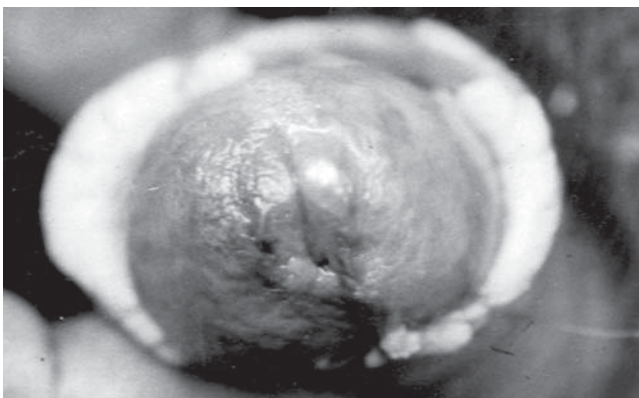


Fig. 1 : Acetowhite areas on glans penis and meatus at 7O'clock position.

of these 38 cases, all of whom were asymptomatic, showed evidence of HPV infection. In the present study the anatomic distribution of HPV lesions in the male genitalia, in majority of cases was present on the glans penis (26.66%), and followed by urethra (17.77%) (Table 1). These lesions in the urethra were diagnosed by cytological examination alone.

### Discussion

In the present study, none of the males had any complaints related to HPV infection which is similar to the findings of Boon et al<sup>10</sup> who studied 20 male consorts of HPV infected females and observed that none of the men were aware of any penile abnormality. Krebs and Schneider<sup>9</sup> observed that 7% of 86 cases in their study had symptoms such as non-healing penile lesions, urethral discharge, bloody ejaculate and penile pruritus. But these symptoms were largely explained by concurrent infection such as gonorrhoea or herpes. While Rosenberg et al<sup>14</sup> observed that the most common complaint in their study of sexually transmitted papilloma viral infection in men was the appearance of penile or perianal papules, but intraurethral condylomas were usually asymptomatic.

In the present study the anatomic distribution of HPV lesions in the male genitalia (Table 1), in majority of cases was present on the glans penis (26.66%), followed by urethra (17.77%). Whereas, in a study conducted by Krebs and Schneider,<sup>9</sup> most of the HPV associated lesions were located in the penile prepuce and almost half of these were at or near the frenulum, while in a study by Rosenberg et al,<sup>14</sup> 42% of the visible HPV associated lesions were located on the penile shaft alone.

The observation by other workers<sup>9, 15</sup> that clinical examination alone was not contributory in the detection of HPV cases was confirmed in the present

**Table 1 : Anatomic distribution of HPV lesions in male genitalia diagnosed by cytology and penioscopy**

Distribution	Cases
Urethra*	3
Urethral meatus	1
Glans penis	4
Corona	1
Frenulum	0
Prepuce	1
Shaft	0
Total	10

\*These cases were diagnosed by cytology alone.

study as none showed any evidence of HPV infection on clinical examination. While, 13.16% cases were positive after penioscopy alone, 7.90% cases were positive by cytology alone, and 5.26% cases were positive by a combination of these two methods (Table 2). Whereas, the frequency of detection of HPV infection by penioscopy reported in other studies varied from a low of 9.4%<sup>8</sup> to a high of 100%.<sup>16</sup>

A correlation of the histopathologic diagnosis of cervical biopsies in women and the results of the different tests in their male consorts, showed that 7 (26.92%) of the males who had HPV infection were detected by cytology and penioscopy. 6 (26%) of these cases were male consorts of 23 females who had a histopathologic diagnosis of CIN I/HPV infection. Four of these cases were diagnosed by penioscopy after acetic acid test and two by cytology. One (50%) male consort of the females with CIN II/HPV infection had HPV infection, which was detected by penioscopy with acetic acid test. No HPV infection was detected in the (single) male consort of the female who had CIN III/HPV infection (Table 3). Barrasso et al<sup>17</sup> reported that 41.2% males had condylomas and 5.4% were histologically positive for HPV infection when their female consorts were suffering from CIN. When acetic acid application test (positive in 22%) and penioscopy

(positive in 42.5%) was taken into consideration a total of 64.4% cases were positive for HPV infection in the same study.

Urine cytology study by Levine et al<sup>7</sup> helped to detect HPV infection in 64, 16 and 50 percent of the men whose female partners had CIN I/condyloma, CIN II and CIN III respectively, while Krebs and Schneider<sup>9</sup> detected HPV infection by histology in 66, 67 and 60 percent of male consorts of females with CIN I, CIN II and CIN III respectively. A comparison of these findings with the present observations confirms the observation of Krebs and Schneider<sup>9</sup> that the grade of CIN (I to III) of the female partner has no influence on either the frequency or the histology of penile lesions.

There are various cytologic features that are indicative of HPV infection. These features include koilocytosis, dyskeratosis, hyperkeratosis, parakeratosis and multinucleation. These features individually are only indicative but not specific of HPV infection (except koilocytosis). Combinations of two or more cytologic features are diagnostic of HPV infection.<sup>10,15</sup> Koilocytosis alone and in combination with other features were seen in 2 cases, while dyskeratosis in combination with the other features was observed in 2 cases. Parakeratosis and hyperkeratosis in combination helped to detect a case of HPV infection. Hyperkeratosis alone that was observed in one case is not diagnostic in itself for HPV infection. Other workers too are of the opinion that although koilocytosis is pathognomonic, the other non-classic criteria may help predict HPV infection.<sup>10,12</sup> Cecchini et al<sup>15</sup> reported that these non-classic criteria might often be the only notable change in detecting HPV infection. Boon et al<sup>10</sup> observed hyperkeratosis in all the twenty cases they studied while koilocytosis and parakeratosis was observed in one case and three cases respectively. The reason for absence of koilocytes was thought to be due to a thick layer of keratinised cells covering the koilocytes.<sup>10</sup> Whereas Levine et al<sup>7</sup> attributed the rare presence of koilocytosis in urethral smears to the transitional epithelial lining of the

**Table 2 : Detection of HPV infection by clinical examination, penioscopy, urethral cytology and by combination of these methods**

HPV infection	Cases	
	No.	%
No evidence of HPV infection by any method	28	73.68
Evidence of HPV infection	10	26.32
• Clinical examination	0	-
• Penioscopy with acetic acid application	05	13.16
• Cytology	03	7.90
• Methods in combination		
o Clinical examination and penioscopy	0	-
o Clinical examination and cytology	0	-
o Penioscopy and cytology	02	5.26
o Clinical examination, penioscopy and cytology	0	-

**Table 3 : Histopathological diagnosis of cervical biopsies in women, and results of different tests in their male consorts**

Diagnosis in females	Total no. of females	Males positive for HPV			
		Clinical examination	Penioscopy (with acetic acid)	Cytology	Total
CIN I/HPV	23	Nil	4	2	6
CIN II/HPV	2	Nil	1	Nil	Nil
CIN III/HPV	1	Nil	Nil	Nil	1
Total	26	Nil	5	2	7

urethra, which may undergo squamous metaplasia, and viral infection of the metaplastic epithelium will usually not result in the production of characteristic koilocytes. Other reasons that could account for the frequent absence of koilocytes in the cytologic smears are that the cytologic specimen usually contains only the superficial layer of the lesion in which there are no koilocytes, and the frequency of koilocytes in the deep layer is much less than that in the cervix.

The close relation of HPV infection to cervical intraepithelial neoplasia and its venereal nature strongly suggests the role of men as vectors of oncogenic HPV types. But the tendency for penile condylomata to be clinically inapparent explains why this association was not recognized until recently. This makes it imperative to screen all male consorts of females with HPV infection with or without CIN. But routine screening of sexually active males is hampered by the lack of a simple, convenient and effective screening technique. Methods like urine cytology and cytological evaluation of smears from the external skin of the penis and scrotum results in low yield of cells. By contrast, smears obtained from the male urethra by cotton swabs or cytobrush results in satisfactory cellularity and therefore a higher rate of HPV detection. Hence urethral cytology should be routinely used in association with penoscopy as a screening test for the detection of HPV infection.

## References

1. Cartwright RA and Sinson JD. Carcinoma of penis and cervix. *Lancet* 1980; 1: 97.
2. Li JY, Li FP, Blot WJ, et al. Co-relation between cancers of uterine cervix and penis in China. *J Natl Cancer Inst* 1982; 69: 1063-5.
3. MacGregor JE and Innes G. Carcinoma of penis and cervix. *Lancet* 1980; 1: 1246-7.
4. Graham S, Priore R, Graham M, et al. Genital cancer in wives of penile cancer patients. *Cancer* 1979; 44: 1870-4.
5. Martinez I. Relationship of squamous cell carcinoma of the cervix uteri to squamous cell carcinoma of the penis among Puerto Rican women married to men with penile carcinoma. *Cancer* 1969; 24: 777-80.
6. Smith PG, Kinlen LJ, White GC, et al. Mortality of wives of men dying with cancer of the penis. *Brit J Cancer* 1980; 41: 422 - 8.
7. Levine RU, Crum CP, Herman E, Silvers D, Ferenczy A, Richart RM. Cervical papilloma virus infection and intraepithelial neoplasia: a study of male sexual partners. *Obstet Gynecol* 1984; 64: 16-20.
8. Sedlacek TV, Cunane M, Carpinello V. Colposcopy in the diagnosis of penile condyloma. *Am J Obstet Gynaecol* 1986; 154: 494-6.
9. Krebs HB and Schneider V. Human papillomavirus - Associated lesions of the penis: colposcopy, cytology and histology. *Obstet Gynecol* 1987; 70: 299 - 304.
10. Boon ME, Schneider A, Hogewoning CJA, Kwast H, Bolhuis P, Kok LP. Penile studies and heterosexual partners: penoscopy, cytology, histology and immunocytochemistry. *Cancer* 1988; 61: 1652 - 9.
11. Krebs HB. Genital HPV infections in men. *Clin Obstet Gynecol* 1989; 32: 180 - 90.
12. Gupta J, Gupta P, Shah K. Detection of human papilloma virus in cervical smears: a comparison of in situ hybridization, immunocytochemistry and cytopathology. *Acta Cytol* 1987; 31: 387 - 96.
13. Crum CP. Papilloma- related changes and premalignant and malignant squamous lesions of the uterine cervix. In: Clement PB and Young RH, editors. Contemporary issues in surgical pathology. Tumor and tumor-like lesions of the uterine corpus and cervix. 1st ed. New York: Churchill Livingstone; 1993. p.51-83.
14. Rosenberg SK, Greenberg MD, Reid R. Sexually transmitted Papilloma viral infection in men. *Obstet Gynecol Clin North Am* 1987; 14: 495 - 512.
15. Cecchini S, Cipparrone I, Confortini M, et al. Urethral cytology of cytobrush specimens: a new technique for detecting subclinical human Papilloma virus infection in men. *Acta Cytol* 1988; 32: 314-7.
16. Brinton LA, William CR, Maria MB, et al. The male factor in the etiology of cervical cancer among sexually monogamous women. *Int J Cancer* 1989; 44: 199-203.
17. Barrasso R, DeBrux J, Odile C and Orth G. High prevalence of HPV associated penile intraepithelial neoplasia in sexual partners of women with cervical intraepithelial neoplasia. *N Engl J Med* 1987; 317: 916-92.