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# O R I G I N A L Prevalence of abnormal Papanicolaou smears in R T I C L F female sex workers in Hong Kong

KM Leung 梁啟文 Gary PS Yeoh 楊佩成 Objective To investigate the prevalence of pre-cancerous uterine cervix HN Cheung 章曉妮 lesions as detected in Papanicolaou (Pap) smears from female Francois Y Fong 方 陽 sex workers in Hong Kong. KW Chan 陳健慧 Design Retrospective analysis of laboratory records. Private anatomical pathology laboratory, Hong Kong. Setting Female sex workers undergoing Pap smear examinations at two Patients non-governmental organisations between 2006 and 2012. Detection of pre-cancerous uterine cervical conditions and Main outcome measures their management. A total of 2697 satisfactory Pap smears from female sex workers Results were performed during the study period from 2006 to 2012. In these subjects, the point prevalence of low-grade squamous intraepithelial lesion and atypical squamous cells of unknown significance was 10.12% (compared with 3.92% for the general population during the same period), whereas that of high-grade squamous intraepithelial lesions and atypical squamous cells of unknown significance with or without high-grade intraepithelial lesions was 2.22% (compared with 0.54% in the general population). For both categories of lesions, the higher prevalence among female sex workers than in the general population was statistically significant. Most patients who had abnormal Pap smears received proper referrals and follow-up management according to recommended guidelines. Conclusions Female sex workers in Hong Kong as a group had a significantly higher prevalence of abnormal Pap smears than the general population. Non-governmental organisations providing freeof-charge screening services to these women helped early detection and proper follow-up for those who had abnormal Pap smears, whilst also increasing their awareness of women's health issues.

Key words Sex workers; Uterine cervical neoplasms; Vaginal smears

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New knowledge added by this study

Female sex workers in Hong Kong have a higher prevalence of abnormal Pap smears than in the general population, and are therefore at higher risk of developing cervical cancer. Implications for clinical practice or policy

Health education, vaccination, and screening services should be made readily available to this group of subjects.

# Introduction

Cervical cancer is the fifth most common cancer in women worldwide, with approximately 471 000 new cases diagnosed each year.<sup>1</sup> Since its introduction in 1941, Papanicolaou (Pap) smear screening is believed to have reduced the number of cervical cancer-related deaths by approximately 74% or by approximately 2% per year.<sup>2</sup> This improvement was seen in nearly every country promoting women's awareness and participation in cervical health screening programmes, making it the most successful health screening programme of the century against cancer.

In Hong Kong, cervical cancer is the sixth commonest cancer among females; in 2009 it accounted for 3.7% of all new cancers in females.<sup>1</sup> In most patients, cervical cancers are related to human papillomavirus (HPV) infection. Many HPV infections are temporary

## 香港女性性工作者中子宮頸抹片異常的患病率

- **目的** 探討香港女性性工作者中,從子宮頸抹片結果找出癌 前宮頸病變的患病率。
- 設計 實驗室紀錄的回顧性分析。
- 安排 香港一所私家病理解剖實驗室。
- **患者** 2006年至2012年期間於兩所非政府組織接受子宮頸 抹片檢查的女性性工作者。
- 主要結果測量 癌前宮頸的檢測及處理。
  - 結果 2006至2012年研究期間,共2697名女性性工作者進行子宮頸抹片檢查。當中發現低度鱗狀上皮內病變和未明確診斷意義的非典型鱗狀上皮細胞的時點患病率為10.12%(同期一般人口為3.92%);而高度鱗狀上皮內病變以及未明確診斷意義的非典型鱗狀上皮細胞(有或無高度鱗狀上皮內病變)的時點患病率則為2.22%(一般人口為0.54%)。有關這兩類病變,女性性工作者比一般人口明顯有較高發病率。大多數有子宮頸抹片異常的患者都按建議準則被轉介作跟進。
    - 結論 香港女性性工作者子宮頸抹片異常的情況明顯比一般 人口的患病率較高。非政府組織提供的免費檢查服務 有助婦女子宮頸抹片異常的早期診斷和適當跟進,同 時也提高她們的意識及對婦女健康問題的關注。

and have little long-term significance. Two thirds of such infections resolve within 1 year and 90% within 2 years. However, in 5 to 10% of women, the infection persists and leads to an increased risk of precancerous lesions of the cervix, which can progress to invasive cancer. This process usually takes 10 to 15 years, providing many opportunities for detection and early intervention. Thus, progression to invasive cancer can almost always be prevented by good prevention strategies.

Regarding HPV transmission, it cannot be entirely prevented by the use of condoms as there may still be contact between uncovered genital areas of the partners. Studies have shown that the use of condoms offers a protection rate of about 70%.<sup>3</sup> The popularity of condom use increased sharply since the era of acquired immunodeficiency syndrome, for which it is a primary prevention strategy. We conducted this study to discover the prevalence of HPV-related lesions as detected in Pap smears from female sex workers and compared it with that in the general population of Hong Kong. Based on a much smaller data set, our previous study showed that the point prevalence of Pap smear-diagnosed cervical intraepithelial neoplasia of all grades (I-III) in female sex workers in Hong Kong was 9.8%.4 We had also reported a corresponding prevalence in our general population (estimated over a 6-month period

when we first launched our liquid-based Pap smear cytology test).<sup>5</sup>

Our laboratory provided free-of-charge Pap smear tests to two non-governmental organisations (NGOs) providing services and support for female sex workers in Hong Kong since 2006 and 2009, respectively. Pap smear screening is only one of the many health services they provide to these clients. Other health services provided include human immunodeficiency virus, syphilis, chlamydia, and gonorrhoea screening.

#### Methods

This was a retrospective study conducted by retrieving and analysing data in our laboratory information system. Sample collection started from 2006 when one of the NGOs began the Pap smear screening service focusing on female sex workers, which continued till August 2012. Our laboratory is accredited for performing Pap smear tests by the Hong Kong Laboratory Accreditation Scheme of the Hong Kong Accreditation Service. The ThinPrep Pap test liquid-based system was used, and since January 2012, the ThinPrep Imaging System for the dual screening Pap test was implemented. The study group consisted of 2697 satisfactory Pap smear tests from sex workers. Based on 62.2% of the subjects who disclosed their ages, their mean age, standard deviation, and age range were 37, 7, and 18 to 62 years, respectively. According to statistics from various NGOs, around 85% of the female sex workers were born in mainland China but were permanent Hong Kong residents; 10% were from mainland China and had double-entry visas, and 5% were from South-East Asia (mainly the Philippines and Thailand). However, we do not have information regarding the place of origin of individual subjects and no data on their rate of condom use. The control group consisted of 476 066 satisfactory Pap tests sent from our regular referring clinicians during the same period. Since the prevalence of HPV infection may vary with age, in order to match the study group we selected smears from patients aged between 18 and 62 (mean, 45; standard deviation, 9) years. Our regular patient samples were sent by gynaecologists and general practitioners in private practice, as well as from outpatients and in-patients attending private hospitals.

All Pap smears were first screened by cytotechnologists who conformed with the standards for the membership of the International Academy of Cytology, and were then examined by pathologists using the 100% rapid screening protocol. All smears were reported by pathologists according to the *Bethesda system for reporting cervical cytology.*<sup>6</sup> A test was considered abnormal when atypical squamous cells of unknown significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL),

atypical squamous cells of unknown significance with or without high-grade intraepithelial lesions (ASC-H), high-grade squamous intraepithelial lesion (HSIL), atypical glandular cells, adenocarcinoma in situ, or any invasive carcinoma was detected. Abnormal Pap smears of other than ASCUS and LSIL were also double checked by two pathologists before the report was issued. Pearson's  $\chi^2$  test was used for comparison of groups, and P values of <0.05 were considered significant. All patients with abnormal Pap smear results were contacted for follow-up visits and according to log books and computer records of the respective NGOs, over 90% could be recalled for review visits.

## Results

Of the 2697 satisfactory Pap smears from the study group, 336 (12.46%) were abnormal, compared to 4.52% in the control group (P<0.0001). Among the abnormal results, 168 (6.23%) were ASCUS, compared with 2.12% in the controls (P<0.0001); 105 (3.89%) were LSIL, compared with 1.80% in the controls (P<0.0001); 12 (0.44%) were ASC-H, compared with 0.13% in the controls (P<0.0001); 48 (1.78%) were HSIL or squamous cell carcinoma, compared with 0.41% in the controls (P<0.0001); and 3 (0.11%) were glandular lesions, compared with 0.06% in the general population (P=0.3295) [Table].

Counselling and further management were offered by volunteer medical doctors or nurses to subjects with abnormal results. Management was in accordance with the Hong Kong College of Obstetricians and Gynaecologists guidelines.<sup>7</sup> Patients with ASCUS returned to repeat a Pap smear 4 months later. Patients with LSIL or more advanced disease were referred to specialists for colposcopy. Patients with infection returned for a Pap smear 3 months after treatment.

#### Discussion

Being predominantly a sexually transmitted infection, HPV infection and therefore pre-cancerous

conditions of the cervix are expected to be more prevalent in sex workers. Studies from both the developed and developing countries have confirmed this, which suggests that sex workers should have more frequent Pap smears.8-11 It is also known that the disparity between the HPV infection rates in sex workers and the general population varies considerably depending on the country. In Japan, the prevalence of high-risk HPV infection in female sex workers as detected by DNA methodology was 48%, as compared with only 6% in the general population,<sup>11</sup> while in Australia, there was no significant difference.<sup>12</sup> This disparity is thought to be related to certain risk-taking behaviours in the respective regions, particularly the use of condoms. According to our current study, the prevalence of abnormal Pap smears in the general population was very similar to that reported in 1999 in our previous study.5 In another study we conducted,4 based on a smaller sample of 235 subjects, the prevalence of cervical intraepithelial neoplasia of all grades (I-III) combined in female sex workers was 9.8%. While in the current study, the prevalence in this group was 5.67% (LSIL + HSIL). It is difficult to conclude whether this difference was due to a difference in sample size or indicated a genuine decrease in prevalence. The prevalence of actual HPV infection, as detected by viral DNA or other molecular methods, is always higher than the rate estimated from cytological abnormalities (detected in Pap smears), since most patients harbouring the infection do not show the characteristic cytological changes. Although DNA and other molecular tests are more expensive, if resources are available, they could be beneficial to sex workers (a group at increased risk) and ultimately the whole community. Recent studies also suggest that self-collected HPV-DNA sampling may increase the uptake of screening and facilitate triage for those who should have additional Pap smear screening.<sup>13,14</sup> In our laboratory, following the recent introduction of HPV vaccination, requests for HPV-DNA testing were on the rise for women with abnormal Pap smear results. While it is going to take some time to fully understand the impact of HPV vaccination

TABLE. Point prevalence of abnormal Pap smears in sex workers (study group) and in the general population (control group)

Prevalence*	Study group (n=2697)	Control group (n=476 066)	P value (Pearson's $\chi^2$ )
ASCUS	168 (6.23%)	10 094 (2.12%)	<0.0001
LSIL	105 (3.89%)	8579 (1.80%)	<0.0001
ASC-H	12 (0.44%)	609 (0.13%)	<0.0001
HSIL or squamous cell carcinoma	48 (1.78%)	1943 (0.41%)	<0.0001
Glandular lesions	3 (0.11%)	303 (0.06%)	0.3295
All lesions	336 (12.46%)	21 528 (4.52%)	<0.0001

\* ASCUS denotes atypical squamous cells of unknown significance, LSIL low-grade squamous intraepithelial lesion, ASC-H atypical squamous cells of unknown significance with or without high-grade intraepithelial lesions, and HSIL high-grade squamous intraepithelial lesion

on reducing the cervical carcinoma rate, it has definitely become a new motivational factor that has aroused woman's interest and awareness about the importance of cervical cancer screening by means of Pap smears and HPV-DNA testing.

#### Conclusions

This study confirms that HPV-related pre-cancerous

#### References

- 1. Hong Kong Department of Health. Statistics of cervical cancer. Available from: http://www.cervicalscreening.gov. hk/english/sr/sr\_statistics\_cc.html. Accessed Jul 2012.
- 2. Armstrong EP. Prophylaxis of cervical cancer and related cervical disease: a review of the cost-effectiveness of vaccination against oncogenic HPV types. Am J Manag Care 2010;16:217-30.
- Winer RL, Hughes JP, Feng Q, et al. Condom use and the risk of genital human papillomavirus infection in young women. N Engl J Med 2006;354:2645-54. cross ref
- Wong WC, Wun YT, Chan KW, Liu Y. Silent killer of the night: a feasibility study of an outreach well-woman clinic for cervical cancer screening in female sex workers in Hong Kong. Int J Gynecol Cancer 2008;18:110-5. cross ref
- 5. Yeoh GP, Chan KW, Lauder I, Lam MB. Evaluation of the ThinPrep Papanicolaou test in clinical practice: 6-month study of 16 541 cases with histological correlation in 220 cases. Hong Kong Med J 1999;5:233-9.
- 6. Solomon D, Nayar R. The Bethesda system for reporting cervical cytology: definitions, criteria, and explanatory notes. 2nd ed. New York: Springer; 2004.
- HKCOG Guidelines No. 3: guidelines on the management of abnormal cervical cytology. Hong Kong College of Obstetricians and Gynaecologists; 2008.
- 8. Piper MA, Severin ST, Wiktor SZ, et al. Association of human papillomavirus with HIV and CD4 cell count in women

lesions of the uterine cervix are more prevalent in female sex workers than in the general population of Hong Kong. The difference is more pronounced for higher- than lower-grade lesions. The provision by NGOs of non-discriminating and stress-free services and support for this underprivileged group of subjects could help early detection of pre-cancerous lesions and lead to reduced morbidity and mortality in these individuals as well as in the community.

with high or low numbers of sex partners. Sex Transm Infect 1999;75:253-7. cross <sup>ref</sup>

- Hernandez BY, Vu Nguyen T. Cervical human papillomavirus infection among female sex workers in southern Vietnam. Infect Agent Cancer 2008;3:7. cross ref
- Gitsch G, Kainz C, Reinthaller A, Kopp W, Tatra G, Breitenecker G. Cervical neoplasia and human papilloma virus infection in prostitutes. Genitourin Med 1991;67:478-80.
- 11. Ishi K, Suzuki F, Saito A, Kubota T. Prevalence of human papillomavirus, chlamydia trachomatis and *Neisseria gonorrhoeae* in commercial sex workers in Japan. Infect Dis Obstet Gynecol 2000;8:235-9.
- Tideman RL, Thompson C, Rose B, et al. Cervical human papillomavirus infections in commercial sex workers risk factors and behaviours. Int J STD AIDS 2003;14:840-7. cross<sup>ref</sup>
- 13. Snijders PJ, Verhoef VM, Arbyn M, et al. High-risk HPV testing on self-sampled versus clinician-collected specimens: a review on the clinical accuracy and impact on population attendance in cervical cancer screening. Int J Cancer 2013;132:2223-36. cross ref
- Quincy BL, Turbow DJ, Dabinett LN. Acceptability of selfcollected human papillomavirus specimens as a primary screen for cervical cancer. J Obstet Gynaecol 2012;32:87-91. cross<sup>ref</sup>