

Gynecologic infections seen in ThinPrep cytological test in Wuhan, China

Hang Zhou^{1,2,*}, Yao Jia^{1,*}, Jian Shen³, Shaoshuai Wang¹, Xiong Li¹, Ru Yang¹, Kecheng Huang¹, Ting Hu¹, Fangxu Tang¹, Jin Zhou¹, Jingping Yuan³, Lei Huang³, Xun Tian³, Zhilan Chen¹, Qinghua Zhang^{1,3}, Changyu Wang¹, Ling Xi¹, Dongrui Deng¹, Hui Wang¹, Ding Ma¹, Shuang Li (✉)¹

¹Cancer Biology Research Center, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China; ²Department of Obstetrics and Gynecology, Nanjing Drum Tower Hospital, Nanjing University Medical School, Nanjing 210008, China; ³Department of Gynecology and Obstetrics, the Central Hospital of Wuhan, Wuhan 430014, China

© Higher Education Press and Springer-Verlag Berlin Heidelberg 2014

Abstract This study aimed to analyze the prevalence of bacterial, *Candida*, *Trichomonas*, and human papillomavirus (HPV) infections in ThinPrep cytological test (TCT) performed on women of Wuhan, China. ThinPrep smears were screened by two independent experienced pathologists and reported from 2008 to 2010. A total of 46 866 ThinPrep smears were studied, and smears with inflammation were analyzed. Of the 44 162 enrolled patients, inflammation changes were observed in 21 935 (49.7%) and specific infections in 6884 (31.4%). The infections detected were as follows: bacteria, 5663 (82.3%); *Candida*, 825 (12.0%); *Trichomonas*, 273 (4.0%); and HPV, 148 (2.1%). Significant changes were found in the prevalence of bacteria and *Candida* among women who underwent TCT before and after 2010. χ^2 revealed an increasing proportion of specific infections found in smears after 2010 ($P=0.000$). In conclusion, bacterial infection was the most detectable in the ThinPrep smears, followed by *Candida* and *Trichomonas*. The prevalence of infection identified by TCT was found to be similar in previous literature in China.

Keywords ThinPrep cytological test; human papillomavirus; *Candida* infection; *Trichomonas* infection; bacterial infection

Introduction

ThinPrep cytological test (TCT) as a screening method has significantly decreased the incidence of cervical cancer [1]. Cytological results in TCT have a key function in the diagnosis of cervical lesions, so this procedure is routinely offered to women visiting hospitals as an opportunistic screening method. As an added advantage, diagnosis of microbial infection is performed in TCT [2,3]. Bacterial infection reportedly acts as a trigger co-factor in the carcinogenesis of cervical cancer [4]. China is currently facing a lifestyle change with modern trends [5]. However, TCT results about gynecologic infections have only been occasionally reported, and studies have mostly focused on human papillomavirus (HPV) detection [6,7]. This study was performed to determine the prevalence and the pattern of

gynecologic infections, especially bacteria, *Candida*, *Trichomonas*, and HPV, in a hospital setting and to identify the spectrum of these agents seen among women in Wuhan.

Materials and methods

This research constitutes a retrospective study reviewing previous TCT smears in Tongji Hospital and the Central Hospital of Wuhan satisfactory for cytological analysis between July 2008 and June 2010. The cytological reports were accomplished according to the modified Bethesda System (TBS) 2001. The specific infection included bacteria, *Candida*, *Trichomonas*, and HPV. The diagnosis of these infections was based on the typical cellular changes shown in Fig. 1. The non-specific infection consisted of benign and reactive cellular changes associated with inflammations.

Statistical analysis was performed using the statistical software package SPSS version 13.0 (SPSS, Chicago, IL). Categorical variables, such as bacterial, *Trichomonas*, and *Candida* infection rates, among different years were com-

Received August 12, 2013; accepted December 30, 2013

Correspondence: lee5190008@126.com

*Hang Zhou and Yao Jia contributed equally to this manuscript.

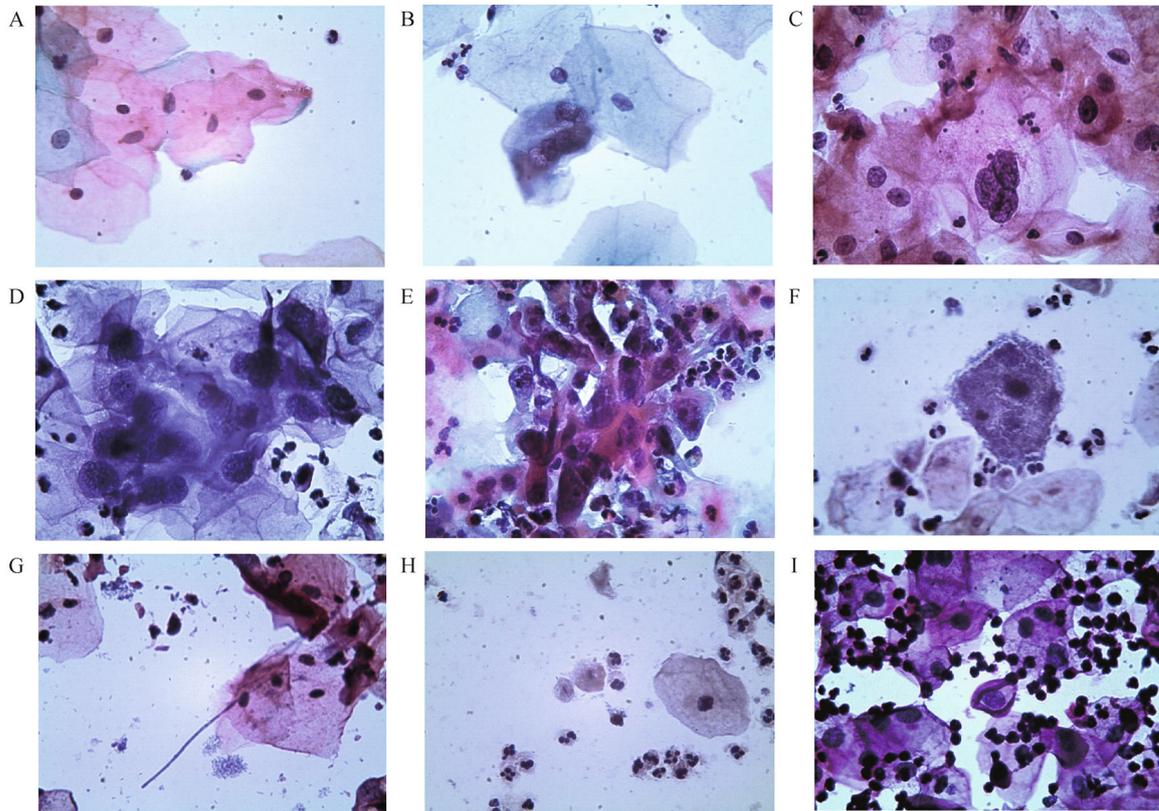


Fig. 1 Photomicrograph of TCT showing the cytological results as NILM, ASC, ISIL, HSIL, and SCC (A–E), and showing the infection of bacteria, *Candida*, *Trichomonas*, and HPV (F–I) (Papanicolaou stain, × 400).

Table 1 ThinPrep smears examined during 2008–2010

Diagnosis	2008	2009	2010	Total
ThinPrep smears	11 477	22 757	9928	44 162
ThinPrep smears with inflammation*	4492 (39.1%)	10 347 (45.5%)	7096 (71.5%)	21 935 (49.7%)
ThinPrep smears with non-specific inflammation**	3417 (76.1%)	7640 (73.8%)	3994 (56.3%)	15 051 (68.6%)
ThinPrep smears with specific infections	1075 (23.9%)	2707 (26.2%)	3102 (43.7%)	6884 (31.4%)

* Percentage with respect to the number of ThinPrep smears.

** Percentage with respect to the number of ThinPrep smears with inflammation.

pared using Chi-square test. A probability value of $P < 0.05$ was considered statistically significant.

Results

Evaluation of inflammation by year

Among the 46 866 cases receiving TCT, 2688 cases were excluded due to incomplete data. Another 16 cases whose cytological results were atypical glandular cells or adenocarcinoma were also excluded. This screening process yielded 44 162 cases which were finally included in the statistical analysis. The mean age of the patients enrolled was

38.68 ± 10.00 years (aged 16 to 86), whereas the mean ages were 38.36 ± 9.98 , 38.70 ± 9.92 , and 38.97 ± 10.17 years in 2008, 2009, and 2010, respectively.

The proportions of ThinPrep smears with specific infections and non-specific inflammation were 31.4% and 68.6%, respectively. The proportion of specific infections increased from 23.9% in 2008 to 43.7% in 2010 (Table 1).

The distribution of specific infections is shown in Table 2. Among the 6884 ThinPrep smears with specific infections, bacterium was detected in 82.3% of smears, *Candida* in 12.0%, *Trichomonas* in 4.0%, and HPV in 2.1%. A total of 6869 patients exhibited multiple infections, whereas the other 15 patients had double infections. No triple infections were

Table 2 Distribution of specific infections seen in ThinPrep smears

Type	2008	2009	2010	Total
Bacteria	822 (76.5%)	2067 (76.4%)	2774 (89.4%)	5663 (82.3%)
<i>Candida</i>	173 (16.1%)	423 (15.6%)	219 (7.1%)	815 (12.0%)
<i>Trichomonas</i>	31 (2.9%)	168 (6.2%)	74 (2.4%)	273 (4.0%)
Human papillomavirus	53 (4.9%)	58 (2.1%)	37 (1.2%)	148 (2.1%)
Specific infections	1075	2707	3102	6884

observed in our study. Nine cases of multiple infections were observed in 2009, followed by four in 2008, and two in 2010.

The prevalence changes in infectious agents over 3 years were analyzed by comparing the prevalence each year (Table 3). Observations showed an increase in the proportion of specific infections detected by TCT. Significant increase of prevalence was observed in bacterial and *Candida* infections by comparing the prevalence in 2009 to 2008 and 2010 to 2009 ($P = 0.000$ and $P = 0.000$ for bacterial infection, and $P = 0.019$ and $P = 0.038$ for *Candida* infection, respectively). The prevalence of *Trichomonas* and HPV infections increased in 2009 and remained unchanged in 2010 ($P = 0.000$ and $P = 0.945$ for *Trichomonas* infection, and $P = 0.001$ and $P = 0.069$ for HPV infection, respectively).

Evaluation of inflammation by age

The prevalence of specific infections in ThinPrep smears is shown in Table 4. Significant difference was found among

different age groups in all infectious agents. The age group with highest prevalence was further analyzed by comparison with the rest of the patients. Therefore, women aged between 46 and 60 had higher prevalence of bacterial and *Trichomonas* infections than the other patients ($P = 0.000$ and $P = 0.000$, respectively), whereas women under the age of 30 had higher prevalence of *Candida* infection than women older than 30 ($P = 0.000$).

Discussion

Gynecologic infections are common around the world and have become major health concerns in China. Most studies in China focus on cytological results in ThinPrep smears using the revised 2001 Bethesda System [2]. However, none has analyzed the prevalence of infections in TCT, and only occasional reports show the prevalence of various infectious agents using conventional Pap smears at the community level

Table 3 Prevalence change in specific infections in ThinPrep smears

	2008		2009		2010		2009 vs. 2008		2010 vs. 2008		2010 vs. 2009	
	Cases	Prevalence (%)	Cases	Prevalence (%)	Cases	Prevalence (%)	χ^2	P	χ^2	P	χ^2	P
Bacteria	822	7.16	2067	9.08	2774	27.94	36.428	0.000	1644.359	0.000	1948.326	0.000
<i>Candida</i>	173	1.51	423	1.86	219	2.21	5.507	0.019	14.447	0.000	4.325	0.038
<i>Trichomonas</i>	31	0.27	168	0.74	74	0.75	28.930	0.000	24.632	0.000	0.005	0.945
HPV	53	0.46	58	0.25	37	0.37	10.108	0.001	1.010	0.315	3.331	0.069
Specific infections	1075	9.37	2707	11.90	3102	31.24	49.675	0.000	1626.371	0.000	1777.423	0.000

Table 4 Prevalence of specific infections in ThinPrep smears among different age groups

Age (year)	Bacterial infection		<i>Candida</i> infection		<i>Trichomonas</i> infection		Specific infections		Total number
	Cases	Prevalence (%)	Cases	Prevalence (%)	Cases	Prevalence (%)	Cases	Prevalence (%)	
≤30	1168	11.2	244	2.3	49	0.5	1489	14.3	10 437
31–45	3089	13.3	394	1.7	126	0.5	3678	15.9	23 177
46–60	1319	13.8	173	1.8	93	1.0	1617	17.0	9530
≥61	87	8.5	4	0.4	5	0.5	100	9.8	1018
χ^2	55.636		25.582		25.966		54.737		
P	0.000		0.000		0.000		0.000		

Table 5 Comparison of bacterial, *Candida*, and *Trichomonas* infections among studies in China

Type	Author	Year	Area	Prevalence
Bacteria	Zhou <i>et al.</i>	2008–2010	Wuhan	5663/44 162 (12.8%)
	Wang <i>et al.</i> [8]	2008	Beijing	38/551 (7.4%)
	Zhang <i>et al.</i> [9]	2003	Beijing	22.2%
	Xu <i>et al.</i> [10]	2007–2009	Beijing	8.7%
	Tang <i>et al.</i> [11]	2003–2004	Sichuan	308/200 (15.4%)
<i>Candida</i>	Zhou <i>et al.</i>	2008–2010	Wuhan	825/44 162 (1.9%)
	Wang <i>et al.</i> [8]	2008	Beijing	40/551 (7.8%)
	Zhang <i>et al.</i> [9]	2003	Beijing	4.9%
	Xu <i>et al.</i> [10]	2007–2009	Beijing	1.7%
	Tang <i>et al.</i> [11]	2003–2004	Sichuan	176/2000 (8.8%)
<i>Trichomonas</i>	Zhou <i>et al.</i>	2008–2010	Wuhan	273/44 162 (0.6%)
	Wang <i>et al.</i> [8]	2008	Beijing	6/551 (1.2%)
	Zhang <i>et al.</i> [9]	2003	Beijing	2.1%
	Xu <i>et al.</i> [10]	2007–2009	Beijing	1.0%
	Tang <i>et al.</i> [11]	2003–2004	Sichuan	14/2000 (0.7%)

[8–11].

The percentage of ThinPrep smears with inflammation in our research was 49.7%, whereas other studies from the Middle East have reported 34.8% to 79.9% [12–15]. Specific infectious agents were identified in 31.4% of our inflammatory cases, which is higher than that in the Muslim population. The most prevalent infections in our study were bacteria (12.8%), *Candida* (1.9%), and *Trichomonas* (0.6%). Other studies in China showed similar pattern, with bacterial infection being the most prevalent, followed by *Candida* (Table 5).

In our study, the prevalence of HPV infection remains unchanged (Table 3). A significant change in HPV infection was observed before and after 2010. Most studies focusing on HPV infection in China obtain their findings from biological results rather than morphology because the typical morphological changes are not recognized in all HPV infections, especially in early infections, which could cause certain missed diagnoses. Unfortunately, this retrospective analysis lacks the biological results of these ThinPrep smears because the biological test for HPV is not a routine part of TCT.

Bacterial infection was statistically significantly increased in women receiving TCT after 2010 in our study. Findings of other studies reporting on the prevalence of bacterial infection in China vary. Zhang *et al.* [9] showed that the bacterial infection in low-income women was 22.2%, a value much higher than that in medical staff. Therefore, living conditions might contribute to the inconsistency of results of bacterial infection. The prevalence of *Candida* and *Trichomonas* infection was 1.9% and 0.6%, respectively, which were lower than those in previous studies (Table 5). These results may be due to the difference in sample size and bias in enrollment.

Moreover, the peak ages of *Trichomonas*, bacterial, and

Candida infections differed, but were relatively approximate in previous studies [16–22]. The occurrence of cervical inflammation was reportedly associated with microbial infection of genital tract and damage caused by physical and chemical factors. The inflammation resulting from chronic microbial infection can produce non-specific and protective anti-microbial oxidants, which can also be harmful to the host DNA, leading to the occurrence of cancer.

This retrospective study reports on the prevalence of specific infectious agents in ThinPrep smears in Wuhan. Cytological results may be a suitable screening method for infections; however, other definitive diagnostic methods cannot be replaced when available, especially for HPV detection.

Acknowledgements

This study was endorsed by the National Basic Research Program of China (973 Program; No. 2009CB521800) and was supported by grants from the National Natural Science Foundation of China (Nos. 30973472, 81001151, 81071663, 30973205, 30973184, and 81101964).

Compliance with ethics guidelines

Hang Zhou, Jian Shen, Shaoshuai Wang, Xiong Li, Ru Yang, Yao Jia, Kecheng Huang, Ting Hu, Fangxu Tang, Jin Zhou, Jingping Yuan, Lei Huang, Xun Tian, Zhilan Chen, Qinghua Zhang, Changyu Wang, Ling Xi, Dongrui Deng, Hui Wang, Ding Ma, and Shuang Li declare that they have no conflicts of interest. This article does not contain any studies with human or animal subjects performed by any of the authors.

References

- Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011; 61(2): 69–90
- Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, Raab S, Sherman M, Wilbur D, Wright T Jr, Young N; Forum Group Members; Bethesda 2001 Workshop. The 2001 Bethesda System: terminology for reporting results of cervical cytology. *JAMA* 2002; 287(16): 2114–2119
- Bukhari MH, Majeed M, Qamar S, Niazi S, Syed SZ, Yusuf AW, Yusuf NW. Clinicopathological study of Papanicolaou (Pap) smears for diagnosing of cervical infections. *Diagn Cytopathol* 2012; 40(1): 35–41
- Kharsany AB, Hoosen AA, Moodley J, Bagaratee J, Gouws E. The association between sexually transmitted pathogens and cervical intra-epithelial neoplasia in a developing community. *Genitourin Med* 1993; 69(5): 357–360
- Zhao FH, Tiggelaar SM, Hu SY, Xu LN, Hong Y, Niyazi M, Gao XH, Ju LR, Zhang LQ, Feng XX, Duan XZ, Song XL, Wang J, Yang Y, Li CQ, Liu JH, Liu JH, Lu YB, Li L, Zhou Q, Liu JF, Zhao N, Schmidt JE, Qiao YL. A multi-center survey of age of sexual debut and sexual behavior in Chinese women: suggestions for optimal age of human papillomavirus vaccination in China. *Cancer Epidemiol* 2012; 36(4): 384–390
- Fan L, Zou LY, Wu YM, Zhang WY. Factors associated with abnormal cervical cytology in pregnant women. *Chin J Obstet Gynaecol (Zhonghua Fu Chan Ke Za Zhi)* 2010; 45(2): 109–113 (in Chinese)
- Belinson JL, Pan QJ, Biscotti C, Wu LY, Pretorius RG, Li L, Elson P, Rong SD, Zhang WH, Qiao YL. Primary screening with liquid-based cytology in an unscreened population in rural China, with an emphasis on reprocessing unsatisfactory samples. *Acta Cytol* 2002; 46(3): 470–474
- Wang XL, Liu ZH, Zhou L, Liao QP, Liu HT. Epidemiological investigation of lower genital tract infectious diseases among women in part of Beijing area. *Chin J Exp Clin Virol (Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi)* 2008; 22(2): 119–121 (in Chinese)
- Zhang LJ, Geng YT, An HY, Gao SY, Zhang L, Cen Y, Zeng G. Investigation on reproductive tract infection among floating married women of childbearing age in Fengtai District in Beijing. *Chin J Epidemiol (Zhonghua Liu Xing Bing Xue Za Zhi)* 2003; 24(8): 678–680 (in Chinese)
- Caiyan X, Weiyuan Z, Minghui W, Songwen Z. Prevalence and risk factors of lower genital tract infections among women in Beijing, China. *J Obstet Gynaecol Res* 2012; 38(1): 310–315
- Yongjun T, Samuelson J, Qingsheng D, Ali MM, Li X, Yanjian M, Xiaoqing C, Jun L, Jian C, Bi L. The prevalence of sexually transmitted and other lower reproductive tract infections among rural women in Sichuan Province, China. *Southeast Asian J Trop Med Public Health* 2009; 40(5): 1038–1047
- Al-Awadhi R, Al-Ramadan BA, George SS, Sharma PN, Kapila K. Gynecologic infections seen in cervical smears in Kuwait. *Acta Cytol* 2010; 54(1): 50–54
- Malkawi SR, Abu Hazeem RM, Hajjat BM, Hajjiri FK. Evaluation of cervical smears at King Hussein Medical Centre, Jordan, over three and a half years. *East Mediterr Health J* 2004; 10(4–5): 676–679
- Wasti S, Ahmed W, Jafri A, Khan B, Sohail R, Hassan S. Analysis of cervical smears in a Muslim population. *Ann Saudi Med* 2004; 24(3): 189–192
- Sullam SA, Mahfouz AA, Dabbous NI, el-Barrawy M, el-Said MM. Reproductive tract infections among married women in Upper Egypt. *East Mediterr Health J* 2001; 7(1–2): 139–146
- Fernando SD, Herath S, Rodrigo C, Rajapakse L. Clinical features and sociodemographic factors affecting *Trichomonas vaginalis* infection in women attending a central sexually transmitted diseases clinic in Sri Lanka. *Indian J Sex Transm Dis* 2012; 33(1): 25–31
- Faber MT, Nielsen A, Nygård M, Sparén P, Tryggvadottir L, Hansen BT, Liaw KL, Kjaer SK. Genital chlamydia, genital herpes, *Trichomonas vaginalis* and gonorrhoea prevalence, and risk factors among nearly 70,000 randomly selected women in 4 Nordic countries. *Sex Transm Dis* 2011; 38(8): 727–734
- Levi AW, Harigopal M, Hui P, Schofield K, Chheng DC. Comparison of Affirm VPIII and Papanicolaou tests in the detection of infectious vaginitis. *Am J Clin Pathol* 2011; 135(3): 442–447
- Eriksson K, Adolfsson A, Forsum U, Larsson PG. The prevalence of BV in the population on the Åland Islands during a 15-year period. *APMIS* 2010; 118(11): 903–908
- Depuydt CE, Leuridan E, Van Damme P, Bogers J, Vereecken AJ, Donders GG. Epidemiology of *Trichomonas vaginalis* and human papillomavirus infection detected by real-time PCR in Flanders. *Gynecol Obstet Invest* 2010; 70(4): 273–280
- Caiyan X, Weiyuan Z, Minghui W, Songwen Z. Prevalence and risk factors of lower genital tract infections among women in Beijing, China. *J Obstet Gynaecol Res* 2012; 38(1): 310–315
- Souza PC, Storti-Filho A, Souza RJ, Damke E, Mello IC, Pereira MW, Svidizinski TI, Lopes-Consolaro ME. Prevalence of *Candida* sp. in the cervical-vaginal cytology stained by Harris-Shorr. *Arch Gynecol Obstet* 2009; 279(5): 625–629