

Comparison of conventional and liquid-based Pap smear methods in the diagnosis of precancerous cervical lesions

Zahra Honarvar, Zahra Zarisfi, Saideh Salari Sedigh & Maryam Masoumi Shahrabak

To cite this article: Zahra Honarvar, Zahra Zarisfi, Saideh Salari Sedigh & Maryam Masoumi Shahrabak (2022): Comparison of conventional and liquid-based Pap smear methods in the diagnosis of precancerous cervical lesions, Journal of Obstetrics and Gynaecology, DOI: [10.1080/01443615.2022.2049721](https://doi.org/10.1080/01443615.2022.2049721)

To link to this article: <https://doi.org/10.1080/01443615.2022.2049721>



Published online: 17 May 2022.



Submit your article to this journal [↗](#)



Article views: 22



View related articles [↗](#)



View Crossmark data [↗](#)

RESEARCH ARTICLE



Comparison of conventional and liquid-based Pap smear methods in the diagnosis of precancerous cervical lesions

Zahra Honarvar^{a,b} , Zahra Zarisfi^a , Saideh Salari Sedigh^a and Maryam Masoumi Shahrbabak^a

^aDepartment of Obstetrics and Gynecology, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran; ^bClinical Research Development Unit, Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran

ABSTRACT

Cervical cancer is one of the five most common cancers among women. The present study aimed to compare conventional and liquid-based Pap smear methods in 2018 in Kerman, Iran. This was a cross-sectional study. Pap smear samples (conventional Pap smear (CN) and liquid-based cytology (LBC)) were collected from five health centres in Kerman. Samples were classified into two groups of liquid and CNs, and each group was classified into normal, abnormal (including, atypical squamous cells of undetermined significance (ASCUS⁺), atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (ASC-H⁺), low-grade squamous intraepithelial lesion (LSIL⁺), high-grade squamous intraepithelial lesion (HSIL⁺) and cancer⁺) and unsatisfactory. Descriptive data analysis and chi-square/Fisher's exact test were performed in SPSS 20 (SPSS Inc., Chicago, IL). Totally, 31,513 women were screened by two CN and LBC. The mean age of subjects was 39.73 ± 9.58 years. The unsatisfactory smears (1.4% versus 0.02%; $p = .001$) and ASCUS⁺ (45.1% versus 39.4%; $p = .007$) were more reported by conventional tests, while LSIL⁺ (33.1% versus 38.9%; $p = .005$) was reported by the LBC test. Among women who were younger than 40 years, the CIN2⁺ that was found by LBC was significantly more than the CN method (37.4% versus 31.7, $p = .04$) and among older women (older than 40 years) the CIN1⁺ was significantly more as well (18% versus 13.6%, $p = .05$). The present study showed that, although LBC had many advantages, CN is still useful. Further studies are to be suggested as a clinical trial in another population with a large number of participants to compare the diagnosing methods of cervical cancers.

KEYWORDS

Pap smear; Papanicolaou test; liquid-based cytology; cervical lesions

IMPACT STATEMENT

- **What is already known on this subject?** The conventional Pap smear (CN) and liquid-based cytology (LBC) methods are the most common methods for screening cervical cancers. Previously, in some studies, LBC was reported as a better method and in some studies, traditional method was preferred. Conflicting results were found in previous articles.
- **What do the results of this study add?** LBC compared to CN could find truer abnormal cases. The superiority of the LBC method is seen in cases such as reducing unsatisfactory cases, etc. LBC compared to CN could find more CIN⁺. Also, LBC could find more CIN1⁺ among women older than 40 years and more CIN⁺ ≥ 2 among younger women.
- **What are the implications of these findings for clinical practice and/or further research?** Although LBC has many advantages and it is easier, CN is still useful and both methods are suitable for cervical abnormality and cancer detection. CN cannot be declared an outdated method.

Introduction

The cancer type and its incidence and mortality rate are varying in different populations and gender. Cervical cancer is one of the five most common cancers among women (Ferlay et al. 2015) and in developing countries, cervical cancer is the second most common cancer after breast cancer (Karimy et al. 2012). Although cervical and uterus cancers are not among the top five cancers in Iranian women (Rafiemanesh et al. 2015; Amori et al. 2017; Farhood et al. 2018), ovarian cancer is one of the 10 most common cancers in Iranian women (Kolahdoozan et al. 2010; Rafiemanesh et al. 2015; Zendehtdel 2019). Also, genital cancers in a woman due to

the unpleasant consequences affect fertility, marital and quality of life (Mohammadi and Ghaffari 2007). Therefore, a reliable method for accurate and timely diagnosis of these diseases in women is essential. Also, the results of the studies have shown that proper and timely screening for genital cancers in women plays an important role in preventing and increasing the survival of them (Khezeli and Dehdari 2012; Bengtsson and Malm 2014).

According to the WHO report, the target age group for cervical cancer screening is 30–40 years (WHO 2018) and the average at diagnosis for this cancer in 2018 was 53 years and ranging from 44 to 68 years globally (Arbyn et al. 2020). The conventional Pap smear (CN) and liquid-based cytology (LBC)

method are the most common methods for screening cervical cancers. The CN method is more common and cheaper in Iran which also has some limitations, including high levels of inadequacy (Curtis et al. 2004; Apgar et al. 2008) and factors such as the use of spatula that transport, less than 20% of the collected epithelial cells onto the slide (Apgar et al. 2008). Also, the distribution of the collected cells differs on the slide, and also to these factors, different skill sets and human errors affect the quality of smears and samples collected, which is the most important stage for evaluation (Mood et al. 2009). In the LBC method, all the collected samples are transferred to a special alcohol-based preservative fluid instead of slides. The sample is sent to the laboratory in this way and it can be stored at ambient temperature for a long time. A homogenous sample is prepared and placed on a slide with the specified boundary, and these cells represent the whole sample (Apgar et al. 2008; Mood et al. 2009).

Many epidemiological studies have shown that cervical cancer screening with a well-screened and population-based screening program can dramatically reduce the incidence and mortality of this disease (Safaeian et al. 2007; Lazcano-Ponce et al. 2008). In recent studies, the results showed that the liquid-based thin-layer method improves the quantity and quality of the samples and reduces unsatisfactory or satisfactory but limited cases (Ensani et al. 2006; Zafari et al. 2010). Meanwhile, the results of a study by Singh et al. in India showed that LBC samples provide better clarity, the invariant spread of smears, less time for screening and better operation of haemorrhagic and inflammatory samples (Singh et al. 2015).

Regarding the necessity of a timely and accurate diagnosis of genital malignancies and considering the efficacy of screening methods in identifying as well as reducing the incidence and mortality of these diseases, the present study aimed to compare conventional and liquid-based Pap smear methods in the largest province of Iran, Kerman.

Materials and methods

Study population and data collection

This was a cross-sectional study that was done during one year. Pap smear samples from five health centres including Afzalipour Hospital, Besat Specialist Clinic, Dr. Dabiri Pathology Laboratory, Tabrizchi Pathology Laboratory and Arad Center Pathology Laboratory were collected during 2018 in Kerman. Samples were classified into two groups of liquid and CNs, and each group was classified into normal, abnormal (including: atypical squamous cells of undetermined significance (ASCUS⁺), atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (ASC-H⁺), low-grade squamous intraepithelial lesion (LSIL⁺), high-grade squamous intraepithelial lesion (HSIL⁺) and cancer⁺) and unsatisfactory. Variables including age, method of contraception, type of Pap smear method and its results were extracted. All patient-related information was confidential and non-invasive intervention was performed on them.

Inclusion and exclusion criteria

Living in Kerman and referring to the five health centres that were mentioned before were inclusion criteria. The cases that previously had abnormal Pap smear or had undergone surgical treatment for precancerous cervical lesions were excluded.

Sampling method

In CNs, the specimens were spread on slides. Liquid prep method was done manually for cytology in liquid medium and materials required for testing were provided by LGM from the USA on behalf of Iran Tasnim Gostar. The professional gynaecologist did all sampling for both methods. In the CN group, wooden spatula and liquid-based method endocervix brushing were used for sampling cervical smears. Smears from the CN method were spread on slides and after fixation sent to the laboratory. The brushes were put in vials containing 5 mL liquid, numbered and then sent to the laboratory. In abnormal Pap smears, the cervical biopsy was collected undergoing colonoscopy, the results (in both conventional and liquid-based Pap smears) were divided into cervical intraepithelial neoplasia (CIN) 1–3, adenocarcinoma *in situ* and cervical cancer groups by pathology. Also, in both the conventional- and liquid-based Pap smears, the concordance between the Pap smear results and the pathology (cervical biopsies performed in abnormal Pap smears) was compared. The Bethesda 2001 system was used for reporting slides.

For cytology in liquid medium, the liquid prep instruction was performed as following: (1) 4 mL of cleaning solution was poured into a centrifuge tube using a serological pipette. (2) The preservative vial was thoroughly stirred using a shaker and the content of it was immediately and carefully added to 4 mL of cleaning fluid in the tube. (3) The numbered tube was placed and centrifuged at 1200×g, for 10 minutes. (4) After centrifugation, the tube was inverted and the fluid was discharged and tube spans were cleaned with a napkin. (5) 500 Landau (0.5 mL) of the cellular base was added to the cell suspension tube. This important fluid caused decapsulation and adhesion of the proper number of cells on the slide. (6) The tube was again stirred with a shaker and then 50 Lg of homogenous suspension was placed on the slide by the smiler. (7) The slides were dried at room temperature and then stained with Pap smear. Finally, the slides were examined microscopically by an assistant and pathologist (in both CN and LBC). The index defined for sufficient specimens in the cytology assay of the squamous cellular fluid medium was at least 5000 cells and the conventional method was at least 8000 cells.

Statistical analysis

Descriptive data analysis and chi-square or Fisher's exact test were performed in SPSS 20 (SPSS Inc., Chicago, IL) and the significant level was considered less than .05.

Ethics approval

This study was approved by the Ethics Committee of Kerman University of Medical Sciences in Iran (ethical code: IR.KMU.REC.1397.038).

Results

Of 31,513 women examined by CN and LBC, CN was performed for more than half of subjects ($n = 17,074$, 54.2%) and others were examined by LBC. According to Pap smear findings, 2330 people with abnormal Pap smear again checked with colposcopy. For 17 persons with the normal Pap smear result, the colposcopy also performed due to the observation of gross tissue during Pap smear procedures. The mean (\pm SD) age of subjects with abnormal Pap smear was 40.60 (10.38) years (age range: 21–82). The liquid-based Pap smear was positive for more than half of the subjects ($n = 1470$, 62.6%) and other positive results were reported by the conventional method ($n = 878$, 37.4%). Unsatisfactory smear was seen in little of subjects ($n = 15$, 0.6%) and the ASCUS⁺ was more prevalent among them ($n = 968$, 41.2%). The results showed that conventional methods in comparison to liquid-based cytology had more unsatisfactory smears (1.4% vs. 0.2%, $p \geq .001$) and reported frequent ASCUS⁺ (45.1% vs. 35.4%, $p \geq .001$). In contrast, LSIL⁺ was more reported by LBC versus conventional method (38.9% vs. 33.1%, $p = .005$). There was no significant difference based on Pap smear findings between the two methods (Table 1).

The results of our study showed that liquid-based method in comparison to CN could find more true cases which was confirmed by colposcopy (65.8% vs. 34.2%, $p = .002$), but there was no significant difference between the frequency of CIN grades in conventional- and liquid-based Pap smear ($p = .88$ for CIN1 and $p = .06$ for CIN ≥ 2) (Tables 2 and 3).

It means LBC compared to CN could find truer abnormal cases in both age groups ($p \leq .001$ and $p = .04$, respectively) (Table 2). Liquid-based Pap smear in contrast to the conventional method was more able to detect true cases confirmed by colposcopy as CIN was ≥ 2 among younger patients who had less than 40 years old (37.4% vs. 31.7%, $p = .04$). For older patients (age ≥ 40 years), this test also was stronger to find true cases confirmed by colposcopy as CIN1 (18% vs. 13.6%, $p = .05$) (Table 3).

In the present study, 18 women reported as cancer patients, while only one of them had an abnormal Pap smear result. The majority of them also detected in biopsy ($n = 15$, 83.3%). Two Pap smear methods in the detection of cancer patients were similar ($p = .89$).

Discussion

In the present study, the unsatisfactory smears were found in a small number of subjects (0.6%) and the ASCUS⁺ was more frequent among them (41.2%). Also, the results showed that the unsatisfactory smears were more reported by conventional tests (1.4%), while ASCUS⁺ and LSIL⁺ were significantly more frequent in LBC cases. Also, in a study by Beerman et al. (2009) in the Netherland, the detection of ASCUS of LBC in detecting cervical cytology lesions was higher. Meanwhile, in a study by Baker (2002) in Hong Kong, the SIL lesions detected by LBC and CN tests were 5.1% and 3.5%, respectively, and the HSIL lesions were 1% and 0.5%, respectively. Also, the detection of ASUS lesions by the LBC method was higher than the CN test. The authors suggested that LBC for detecting the intraepithelial lesions and cervical screening is better than using the CN. In another study by Phaliwong et al. (2018) in Thailand, the results showed that the unsatisfactory smears in CN (52.3%) were higher than LBC (40.5%). These results were similar to the current study that showed the advanced liquid-based method.

In contrast, the result of the studies by Mood et al. (2009) in Tehran and Yousefi (2007) in Mashhad showed that the unsatisfactory smears were significantly higher in the LBC samples in comparison to the CN samples. Also, Mood et al.'s (2009) study showed, there was no significant difference between two methods in terms of ASC. In another study by Karimi-Zarchi et al. (2013) in Yazd, the results showed that the diagnosis of ASCUS using the LBC method was lower in comparison with the CN. Although the differences might be due to the different sample and human skill or errors, the results in the present study agreed with other studies which showed the frequency of inadequate smears was decreased by LBC test (Karnon et al. 2004; Pankaj et al. 2018; Phaliwong et al. 2018).

The results of the present study showed that LBC compared to CN could find more CIN⁺. Also, LBC could find more CIN1⁺ among women older than 40 years and more CIN⁺ ≥ 2 among younger women (less than 40 years). The results of a study by Sigurdsson (2013) in Iceland showed that CIN3⁺ histology was significantly higher in LBC only in women

Table 2. The normal and CIN results of the biopsy in two methods of cervical screening, Kerman, 2018.

Pap smear method	Biopsy findings		<i>p</i> Value
	Normal	CIN ⁺	
CN (871)	456 (40.5)	412 (34.2)	.002
LBC (1460)	669 (59.5)	791 (65.8)	
Prevalence difference	-0.19	-0.31	
(95% CI)	(-0.24, -0.13)	(-0.37, -0.25)	

Table 1. The results of conventional Pap smear in comparison to the liquid-based cytology among screened women, Kerman, 2018.

Pap smear method	Unsatisfactory	ASCUS ⁺	ASC-H ⁺	AGC ⁺	LSIL ⁺	HSIL ⁺
Total	15 (0.6)	968 (41.2)	267 (11.4)	17 (0.7)	856 (36.5)	223 (9.5)
CN (871)	12 (1.4)	393 (45.1)	101 (11.6)	6 (0.7)	288 (33.1)	83 (9.5)
LBC (1460)	3 (0.2)	575 (39.4)	166 (11.4)	11 (0.8)	568 (38.9)	140 (9.6)
Prevalence difference	-0.06	0.05	0.002	-0.001	-0.05	-0.001
(95% CI)	(-0.55, 0.43)	(-0.006, 0.12)	(-0.07, 0.08)	(-0.085, 0.083)	(-0.12, 0.009)	(-0.08, 0.07)
<i>p</i> Value	.001	.007	.86	.85	.005	.96

CN: conventional Pap smear; LBC: liquid-based cytology.

Table 3. The comparison of CIN⁺ cytology findings between Pap smear and liquid-based cytology according to age groups, Kerman, 2018.

Age groups	Pap smear method	Biopsy findings			
		CIN1 ⁺	<i>p</i> Value	CIN ≥ 2	<i>p</i> Value
<40	CN ⁺ (486)	83 (17.1)	.57	154 (31.7)	.04
	LBC ⁺ (727)	135 (18.7)		272 (37.4)	
Prevalence difference (95% CI)		-0.01		-0.05	
≥40	CN ⁺ (390)	53 (13.6)	.05	124 (31.7)	.51
	LBC ⁺ (743)	134 (18)		250 (33.6)	
Prevalence difference (95% CI)		-0.04		-0.01	
Total	CN ⁺ (871)	136 (15.7)	.88	196 (22.5)	.06
	LBC ⁺ (1460)	269 (18.4)		396 (27.1)	
Prevalence difference (95% CI)		-0.02		-0.04	
		(-0.1, 0.04)		(-0.11, 0.02)	

CIN: cervical intraepithelial neoplasia.

under 40 years old. Also, the results of the present study showed that more than 60% of true abnormal cases were detected by LBC in both age groups, while LBC was performed for less than half of the subjects. It could be said that LBC compared to CN could find truer abnormal cases. In contrast, in a study by Phaliwong et al. (2018), the result from CN and LBC for abnormal cervical cytology was 4.8% and 0.2% and for cancer was 5.7% and 0.1%, respectively.

Conclusions

The results of the present study showed that ASCUS⁺ and LSIL⁺ were significantly more frequent in LBC and unsatisfactory smears were more frequent in CN cases. These results confirmed that, although LBC has many advantages, CN is still useful and both methods are suitable for cervical abnormality and cancer detection. Further studies are to be suggested as a clinical trial in another population with a large number of participants to compare the diagnosing methods of cervical cancers.

Acknowledgements

The authors acknowledge the Kerman University of Medical Sciences and all women who participated in the present study.

Disclosure statement

The authors report no conflict of interest.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

ORCID

Zahra Honarvar  <http://orcid.org/0000-0002-1147-5189>

Zahra Zarisfi  <http://orcid.org/0000-0002-4963-4712>

References

- Amori N, Aghajani M, Asgarian F, Jazayeri M. 2017. Epidemiology and trend of common cancers in Iran (2004–2008). *European Journal of Cancer Care* 26:e12449.
- Apgar BS, Brotzman GL, Spitzer M, Ignatavicius D. 2008. *Colposcopy, principles and practice: an integrated textbook and atlas*. Philadelphia: Saunders/Elsevier.
- Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. 2020. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *The Lancet. Global Health* 8:e191–e203.
- Baker JJ. 2002. Conventional and liquid-based cervicovaginal cytology: a comparison study with clinical and histologic follow-up. *Diagnostic Cytopathology* 27:185–188.
- Beerman H, Van Dorst E, Kuenen-Boumeester V, Hogendoorn P. 2009. Superior performance of liquid-based versus conventional cytology in a population-based cervical cancer screening program. *Gynecologic Oncology* 112:572–576.
- Bengtsson E, Malm P. 2014. Screening for cervical cancer using automated analysis of PAP-smears. *Computational and Mathematical Methods in Medicine* 2014:842037.
- Curtis S, Lee C, Willough B. 2004. Are liquid-based pap tests cost effective. *Women Health Primary Care* 7:391–400.
- Ensani F, Ghaemmaghami F, Behtash N. 2006. Comparative study of 140 fluid-based thin layer Papanicolaou smears prepared using Cyto-tek with their cell blocks versus 100 conventional Papanicolaou smears in terms of adequacy. *Hakim Research Journal* 9:22–27.
- Farhood B, Geraily G, Alizadeh A. 2018. Incidence and mortality of various cancers in Iran and compare to other countries: a review article. *Iranian Journal of Public Health* 47:309–316.
- Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. 2015. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International Journal of Cancer* 136:E359–E386.
- Karimi-Zarchi M, Peighambari F, Karimi N, Rohi M, Chiti Z. 2013. A comparison of 3 ways of conventional Pap smear, liquid-based cytology and colposcopy vs cervical biopsy for early diagnosis of premalignant lesions or cervical cancer in women with abnormal conventional pap test. *International Journal of Biomedical Science* 9:205.
- Karimy M, Gallali M, Niknami S, Aminshokravi F, Tavafian S. 2012. The effect of health education program based on health belief model on the performance of Pap smear test among women referring to health care centers in Zarandieh. *Pars of Jahrom University of Medical Sciences* 10:53–59.
- Karnon J, Peters J, Platt J, Chilcott J, McGoogan E, Brewer N. 2004. Liquid-based cytology in cervical screening: an updated rapid and systematic review and economic analysis. *Health Technology Assessment* 8:iii, 1–78.
- Khezeli M, Dehdari T. 2012. Knowledge, attitude and practice of female employees of health network in Guilan-Gharb county about cervical

- cancer and Pap Smear. *Preventive Care in Nursing & Midwifery Journal* 1:43–50.
- Kolahdoozan S, Sadjadi A, Radmard AR, Khademi H. 2010. Five common cancers in Iran. *Archives of Iranian Medicine* 13:143–146.
- Lazcano-Ponce E, Palacio-Mejia LS, Allen-Leigh B, Yunes-Diaz E, Alonso P, Schiavon R, et al. 2008. Decreasing cervical cancer mortality in Mexico: effect of Papanicolaou coverage, birthrate, and the importance of diagnostic validity of cytology. *Cancer Epidemiology, Biomarkers & Prevention* 17:2808–2817.
- Mohammadi S, Ghaffari F. 2007. Sexual dysfunction and its relation to quality of life of female patients with cancer. *Monthly Tehran University Medical Journal* 65:39–46.
- Mood NI, Dehdashti M, Eftekhari Z, Ahmadi S. 2009. The specimen adequacy and atypical squamous cell frequency: conventional versus liquid-based cytology Pap smears. *Tehran University Medical Journal* 67:900–906.
- Pankaj S, Nazneen S, Kumari S, Kumari A, Kumari A, Kumari J, et al. 2018. Comparison of conventional Pap smear and liquid-based cytology: a study of cervical cancer screening at a tertiary care center in Bihar. *Indian Journal of Cancer* 55:80–83.
- Phaliwong P, Pariyawateekul P, Khuakoonratt N, Sirichai W, Bhamarapratana K, Suwannaruk K. 2018. Cervical cancer detection between conventional and liquid based cervical cytology: a 6-year experience in Northern Bangkok Thailand. *Asian Pacific Journal of Cancer Prevention* 19:1331.
- Rafieemaneh H, Rajaei-Behbahani N, Khani Y, Hosseini S, Pournamdar Z, Mohammadian-Hafshejani A, et al. 2015. Incidence trend and epidemiology of common cancers in the center of Iran. *Global Journal of Health Science* 8:146–155.
- Safaeian M, Solomon D, Castle PE. 2007. Cervical cancer prevention—cervical screening: science in evolution. *Obstetrics and Gynecology Clinics of North America* 34:739–760.
- Sigurdsson K. 2013. Is a liquid-based cytology more sensitive than a conventional Pap smear? *Cytopathology* 24:254–263.
- Singh VB, Gupta N, Nijhawan R, Srinivasan R, Suri V, Rajwanshi A. 2015. Liquid-based cytology versus conventional cytology for evaluation of cervical Pap smears: experience from the first 1000 split samples. *Indian Journal of Pathology & Microbiology* 58:17–21.
- WHO. 2018. Cervical cancer: WHO; [cited 2019 Dec 20]. Available from: <https://www.who.int/cancer/prevention/diagnosis-screening/cervical-cancer/en/>
- Yousefi Z, Sharifi N, Ebrahimzadeh S, Anbiaei S. 2007. The prevalence of unsatisfactory smears in liquid-based and conventional Pap smear. *Journal of Gorgan University of Medical Sciences* 9:12–16.
- Zafari M, Behmanesh F, Tofighi M, Âbasi A, Kialashaki A, Aghamohamadi A. 2010. A comparison of fluid-based thin layer Papanicolaou smear and conventional Pap smear. *Journal of Mazandaran University of Medical Sciences* 20:63–70.
- Zendehtdel K. 2019. Cancer Statistics in IR Iran in 2018. *Basic & Clinical Cancer Research* 11.