JOGCR

Prevalence of Abnormal Pap Smear Results Among Women Attending Kosar Hospital in Qazvin, 1392-1396

Khadijeh Elmizadeh[1], Fatemeh Lalooha[2], Hojat Momenzadeh[3], Kimia Mahloojian[4], Hamideh Pakniat [5*]

1. Department of Obstetrics and Gynecology, Oncology fellowship, Clinical Research Development Unit, Kowsar Hospital, Qazvin University of Medical Sciences, Qazvin, Iran.
2. Department of Obstetrics and Gynecology, Clinical Research Development Unit, Kowsar Hospital, Qazvin University of Medical Sciences, Qazvin, Iran.
3. General Practitioner, Clinical Research Development Unit, Kowsar Hospital, Qazvin University of Medical Sciences, Qazvin, Iran.
4. Medical student, Clinical Research Development Unit, Kowsar Hospital, Qazvin University of Medical Sciences, Qazvin, Iran.
5. Department of Obstetrics and Gynecology, Infertility fellowship, Clinical Research Development Unit, Kowsar Hospital, Qazvin University of Medical Sciences, Qazvin, Iran.

*Corresponding author: Hamideh Pakniat. Infertility fellowship, Clinical Research Development Unit, Kowsar Hospital, Qazvin University of Medical Sciences, Qazvin, Iran. PO Box 3419759811, Qazvin, Iran.
Phone: +98-912-1822448; FAX:+98-28-33330534

Address: Kowsar Hospital, Taleghani Ave., PO Box 3419759811, Qazvin, Iran

Email: pakniat110@yahoo.com
Orcid ID: https://orcid.org/0000-0001-9513-7998

Abstract

Background & Objective: The importance of Pap smear in cervical cancer screening is clear. However, yet no organized program has been developed in Iran to screen cervical cancer. Due to the obvious difference in prevalence of cervical cancer in Iran compared to global statistics, it is necessary to further investigate this issue. As pop smear is the most important factor to decrease the mortality and morbidity of cervical cancer in developed countries, it is important to study the results of abnormal Pap smears and the quality of the report in our region.

Materials & Methods: This study was designed retrospectively with reference to the results of Pap smears performed during 3 years from 2016 in the Kosar hospital. The method of collecting samples was census. The results of Pap smears were extracted from the Hospital and 15208 pap smear results were analyzed.

Results: From the 15208 women, 15150 had normal cytology results (99.62%) and 58 women had abnormal cytology (0.38%). The frequency of abnormal cytology was 0.246% (n=37) for atypical squamous cell of undetermined significance (ASCUS), 0.08% (n=12) for low-grade squamous intraepithelial lesion (LSIL), 0.006% (n=1) for ASC cannot exclude high-grade intraepithelial lesion (ASC-H), 0.046% (n=7) for high-grade squamous intraepithelial lesion (HSIL), 0.006 (n=1) for atypical glandular cells (AGC), and 0% (n=0) for invasive cancer. No SCC were found in this study. **Conclusion**: The prevalence of all abnormal results was much lower than other studies; However, in terms of prevalence of abnormalities, the ranking was similar to other studies.In order to obtain more accurate results, it is recommended to study other epidemiological regions.

Key words: Papanicolaou Test, Uterine Cervical Neoplasms, Human Papillomavirus DNA Tests, Early Detection of Cancer

Introduction

Cervical cancer is the fourth prevalent cancer among wemon after breast, colorectal, and lung cancers. It constitutes 6.9 % of all wemon cancers with about 570000 known cases in 2018 around the globe (1).

Cervical cancer is not among 10 prevalent cancers of wemon in Iran and has a prevalence of 1.78 in 100000 population that is very lower than its prevalence in the world (13.1/100000).

It seems that certain religious beleifs and several regulations are important causes of this underreporting in Iran. Furthermore, relegious beleifs could be an obstacle for wemons' referal and screening in health care centers, thus the available information may not be reliable enough (2).

Cervical cancer mortality is completely dependent on HPV vaccination and also screenig programs for early detection of precancerous and cancerous lesions. In this regard, mortality of cervical cancer has decreased 75% in developed countries after conduction of aformentioned interventions (3,4).

Appropriate anatomic access to lesion site during direct cervical examination and long clinical course of the disease has lead to 95% success rate of identification and treatment of pre cancerous leasions. Accordingly, optimal target of screening of cervical cancer is identification of precancerous lesions (5).

Screening of cervical cancer is done by pap smear and high risk HPV assessment.(6-10).

Pap smear, if applied structured and appropriatly, is the most efficient and widespread known screening method that can significantly decrease incidence and mortality of cervical cancer (11).

Two methods are available for obtaining a pop smear, conventional and liquid based. Although liquid based method provides pathologist with more endocervical cells, both methods have the same diagnostic values (12).

Materials and Methods

This study was conducted retrospectively on hospital records. Participants were all wemon for whom pap smear was performed during 2016 to 2019 . Results were collected from hospital laboratory records .

A total of 15231 pap smear results were reviewd. A checklist was used for data collection including age of participants and pop smear results. Cervical cells abnormalities including abnormalities of squamous and glandular cells individually were recorded as ASCUS, ASC-H, LSIL, HSIL, AGC, and SCC based on Bethesda 2014 system. Type of specimen (conventional or liquid based) and satisfactory or unsatisfactory type of specimen were also recorded.

Data was analysed. Descriptive statistics are reported as frequency, mean and standard deviation. Chi-square, ANOVA, and T-test were used for statistical analysis with SPSS version 19 software. Pvalue <0.05 was considered statistically significant.

Results

This study was conducted on cytology samples of 15231 women during 2016-2019. Of the total samples, 23(0.15%) was not appropriate for further assessment and were excluded from the study. Thus, 15208 samples were statistically analysed.

Of the all samples, 15150(99.62%) had no cellular abnormality. Only 58 samples (0.38%) had abnormal cytology results.

According to abnormal results of Bethesda system (2014), different abnormalities of squamous cell and glandular cell were recorded. No squamous cell carcinoma was observed. Frequency of different cellular abnormalities was as follow; ASCUS 37(0.246%) as the most frequent one, LSIL 12(0.08%), and HSIL 7(0.046%). Glandular cell abnormalities and ASCH had the frequency of 1(0.006%) and as described earlier, no squamous cell carcinoma was observed among cellular abnormalities.

Table 2 depicts frequency of cellular abnormalities and comparison of this frequency with standard results. In current study, frequency of all cellular abnormalities was significantly lower than considered standard frequency (PValue: 0.001).

Frequency of the method of sampling, conventional or liquid based, is illustrated in table 3.

9838 (64.68%) of pap smears were collected by conventional and 5370 (35.32%) by liquid based method. Of 58 samples with cellular abnormality, 36(62.1%) were in conventional and 22(37.2%) were in liquid based samples. Accordingly, no significant statistical association was observed between two types of sampling (Pvalue: 0.7).

Mean age of participants with abnormal sample was 42.29(12.1) years. LSIL abnormalities had the highest mean age (43.16(14.05)) followed by ASCUS, HSIL, AGC, and ASCH, respectively. Age range of participants with cellular abnormalities was between 21 to 60 years. No significant relationship was observed in term of age between different abnormal groups (Pvalue: 0.58).

Figure 1 shows age distribution of abnormal samples ranging from 30 to 50 years. Squamous lesions with high grade was diagnosed in this age range. The least abnormal sample was in age range of 70-80 years (1 sample).

4. Discussion

Current study indicated prevalence of 0.38 for abnormal samples. This estimation is very lower than the prevalence reported in Katki et al study in Us, and Rossi et al in Itay and Shim et al in South Korea (13-15). Furthermore, even in comparison with Bayan et al study in Jordan who investigated the prevalence of Abnormal Pap Smears in a population with low prevalence of cervical cancer, our reported prevalence is significantly lower (16). According to these reports prevalence of cervix cancer and precanceruos lesions in current study is verly lower than other geographical regions with significant difference. In this regard, low prevalence of cytological abnormalities may be due to low prevalence of HPV infection in population of the study. Another reason maybe due to false negative reports . This isuue is very important as a report has estimated false negative report of papsmear in US up to 51 percent (17).

True prevalence of precancerous and cancerous lesions of cervix in Iran may not be as low as what we have observed in present study. A study by Turkmen et al from turkey confirms this

hypothesis. In their met analysis on 28 centers with high population in turkey, prevalence of all cellular abnormalities was 5.08% ranging from 0.3% (similar to our report) to 16.64% (18). Therefore, it seems that further investigation in this regard and evaluation of other epidemiological regions of Iran is warranted. Similar studies in Iran have indicated prevalence of 0.22 which is consistent to our study to 4.04 in the study by maleki et al in Zanjan. Thus more studies may change these reports accordingly (19-21).

Current study showed the most prevalent abnormality as ASCUS (63.8%) and then LSIL(20.7%), and the lowest prevalence for SCC and HSIL. In comparison with large population studies in US, Italy, Soth Korea and the ones with lower sample size, overall without concidering the cervical cancer incidence in the study population, the most prevalent cellular abnormalities reported in pop smear are ASCUS and LSIL, respectively and the lowest frequency is for SCCand HSIL (13-15). This is consistant with the results of our study.

However, studies exist in which unexpectedly high prevalence of other cellular abnormalities are reported. In a study in Nigeria, prevalence of HSIL was as high as the prevalence of ASCUS . (22). Another study in Bangladesh, has indicated higher prevalence of LSIL, and then HSIL than other abnormalities. In this study, ASCUS along with AGC were the lowest prevalent lesion even lower than malignant lesions (23). Bayan et al also reported AGC after ASCUS as the second prevalent lesion (16).

As regard the prevalence of different cellular abnormalities, among the studies in Iran, Arab et al, Almasi Nokiani et al and Tajsadat et al had the same results with our study However, Masoumi et al had the lowest prevalence of LSIL inconsistent with our results (19, 24-26). Accordingly, in Bethesda 2014 reporting system, The most prevalent lesions are ASCUS and LSIL, and the lowest ones are SCC and HSIL.

Different studies on cervical cellular abnormalities give different reports and this may depend on social and cultural issues, religious believes and different prevalence of HPV in the population. In communities with uncontrolled sexual contacts there should be more HPV infection specially in the younger groups and subsequently higher prevalenve of cellular abnormalities and also cancer. However, in commuinties with religious beleives on limited sexual contacts such as Islamic communities and Iran ,this is expected that HPV infection and cervical cancer to be lower(16). However this is a hypothesis and to investigate the reality further multi center studies on prevalence of HPV infection on Iranian women is recommended. It is also necessary to have a powerful, organized and meticulous cancer registry system to give a true and reliable information about cervical cancer incidence in Iran.

Suitability of a cytology sample for assessment is defined by number of achieved cell through sampling and is very important.

Quality check of pathologists who report pop smears is an elementary factor to guarantee quality of Bethesda system (23). In this regard, determination of unsatisfactory samples is very important. In current study, the number of unsatisfactory for evaluation samples was 23(0.15%). In this regard, Paolo et al reported 6.1 unsatistactory samples and it was much more than what we reported in our study and along with our report, one study from Romania and yavin et al reported 0.2 and 0.3 unsatisfactory samples respectively.

Different studies have reported different rates of unsatisfactory samples. The most important issue observed in these studies, is that most of these samples were collected by conventional method. Unsatisfactory samples in conventional and liquid based methods are 1-5.9% and 1.1-3.4%, respectively. Moriarfy et al indicates frequency of 1.1 % for unsatisfactory samples (30). Hajson et al has reported 50% increase in unsatisfactory samples by liquid based method consistent with Usefi etl study in Iran (31,32). Current study showed 2 (8.69%) of samples to be unsatisfactory by liquid based method along with large available evidence in this regard (30, 34-36). Reporting of unsatisfactory samples is associated directly with several factors including method of sampling, fixation method, patient condition during sampling, and final assessment by pathologist who determines if the sample is satisfactory or not.

Unsatisfactory samples of present study was unusually very lower than similar studies,The reason can be explained in ti ways. Optimistically, the samples of the study have had an ideal quality for pathological assessment, On the other hand, the reports may not carry on necessary standard frames. So to clarify this difference, further studies seems to be warranted and other possible factors need to be assessed.

Of the total satisfactory samples, 64.68 % were collected with conventional method and 35.32% with liquid based method. Of 58 abnormal samples, 36(62.1%)were collected by conventional method and 22(37.9%) by liquid based method. However, no statistical diffference was observed between the two methods for diagnosis of abnormal lesions (Pvalue:0.7).

It can be said that abnormal cell distribution is in accordance with number of samples with each sample collection method. Thus, ability of diagnosis of cellular abnormality in each sampling method for satisfactory for evaluation samples is equal and not different significantly. It is note worthy that current study was not designed to differentiate diagnostic power of two sampling methods and for such comparison another study with two samples from each participant and further pathological evaluation is required.

Present study estimated mean age of participants with abonormal lesions as 42.3(12.1) years. Mean age of participants with ASCUS and LSIL lesions were 43(1.25) and 43.1(14) years old, respectively and this was higher than mean age observed for all lesions. Lowest mean age was for ASCH (one 24 years old participant). More abnormalities were observed in ages 30-50 years (65.5%). This age distribution is consistent with Basu et al and Diego et al studies (27, 37).

Assessment of age distribution of cervical abnormalities is important as with such information we can recommend appropriate age for screening of cervical cancer. By such information we also can determine high risk ages for cancerous and precancerous lesions and perform evaluation with higher sensitivity in this age group. In previous studies in Iran, cancerous lesions and mortality due to cervical cancer was higher in ages 55 and 60 years. Precancerous lesions was also higher in ages after 30 years consistent with our study. Thus recommending screening of Iranian wemon from age of 30 seems of great value.

Conflicts of interest statement: The authors of this paper declare no conflicts of interest.

Funding: There is no conflict of interest neither between the authors themselves, the Research Department of …….. University of Medical Sciences as the sole financial supporting body, or any pharmaceutical company regarding the materials used in our study.

Acknowledgements:

The authors would also like to especially thank the Clinical Research Development Unit, ……Hospital, …… University of Medical Sciences, ……, Iran.

1. Tables

Table 1. prevalence of abnormalities

Results	Standard	Present study(%)	pvalue
Unsatisfactory	1	0.15	<0.0001
Without abnormality	95.63	99.62	<0.0001
ASCUS	2.8	0.246	<0.0001
ASC-H	0.17	0.006	<0.0001
LSIL	0.97	0.08	<0.0001
HSIL	0.21	0.046	<0.0001
AGC	0.21	0.006	<0.0001
SCC	0.0045	0	_____
Total abnormalities	4.36	0.38	_____

Table 2. number of abnormalities

Type of abnormality	number	frequency
ASCUS	37	63.8
ASC-H	1	1.7
LSIL	12	20.7
HSIL	7	12.1
AGC	1	1.7
SCC	0	0
Total	58	100

Table 3. type of samples

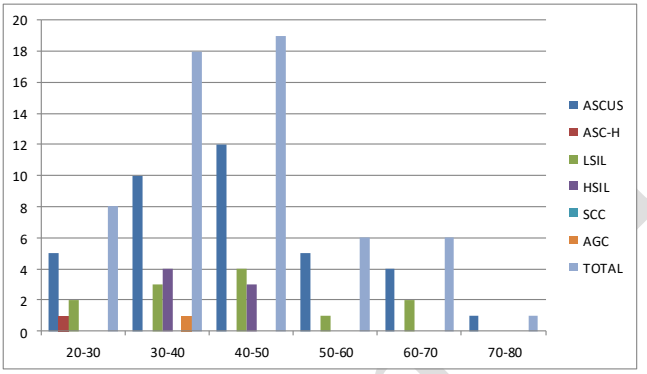
Sample type	Total Number	Percent of Total Number	Abnormalities number	Percent of abnormalities	pvalue
conventional	9838	64.68	36	62.1	0.7
Liquid base	5370	35.32	22	37.9	0.7
Total	15208	100	58	100	-----

Table 4. relationship between age and abnormalities

pvalue	Standard deviation	Age average	number	abnormality
0.58	12.44	43.08	37	ASCUS
0.58	0	24.00	1	ASC-H
0.58	14.05	43.16	12	LSIL
0.58	5.52	39.85	7	HSIL
0.58	0	38.00	1	AGC
0.58	0	0	0	SCC
____	12.10	42.29	58	total

2. Figures

Figure 1: age distribution of cervix abnormalities



References

[1] Freddie Bray, BSc, MSc, PhD1, ME2 Jacques Ferlay, and MD, MSc, PhD3 Isabelle Soerjomataram. "Global Cancer Statistics 2018: GLOBOCAN Estimates." CA CANCER J CLIN, 2018: 1–31

[2] Gholamreza Roshandela, b, Ali Ghanbari-Motlaghc, Elham Partovipourb, Fereshteh Salavatib,. "Cancer incidence in Iran in 2014: Results of the Iranian National Populationbased." Cancer Epidemiology 61 , 2019: 50-58

[3] Quinn M, Babb P, Jones J, Allen E. Effect of screening on incidence of and mortality from cancer of cervix in England: evaluation based on routinely collected statistics. BMJ 1999; 318:904

[4] Willoughby BJ, Faulkner K, Stamp EC, Whitaker CJ. A descriptive study of the decline in cervical screening coverage rates in the North East and Yorkshire and the Humber regions of the UK from 1995 to 2005. J Public Health (Oxf) 2006; 28:355

[5] Saraiya M, Ahmed F, Krishnan S, Richards TB, Unger ER, Lawson HW. Cervical cancer incidence in a prevaccine era in the United States, 1998-2002.Obstet Gynecol. 2007;109(2 Pt 1):360-370

[6] Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol 1999; 189:12

[7] Nobbenhuis MA, Walboomers JM, Helmerhorst TJ, et al. Relation of human papillomavirus status to cervical lesions and consequences for cervical-cancer screening: a prospective study. Lancet 1999; 354:20

[8] Kjaer SK, van den Brule AJ, Paull G, et al. Type specific persistence of high risk human papillomavirus (HPV) as indicator of high grade cervical squamous intraepithelial lesions in young women: population based prospective follow up study. BMJ 2002; 325:572

[9] Wallin KL, Wiklund F, Angström T, et al. Type-specific persistence of human papillomavirus DNA before the development of invasive cervical cancer. N Engl J Med 1999; 341:1633

[10] Committee on Practice Bulletins—Gynecology. Practice Bulletin No. 168: Cervical Cancer Screening and Prevention. Obstet Gynecol 2016; 128:e111. Reaffirmed 2018

[11] Dobbs SP, Asmussen T, Nunns D, Hollingworth J, Brown LJ, Ireland D. Does histological incomplete excision of cervical intraepithelial neoplasia following large loop excision of transformation zone increase recurrence rates? A six year cytological follow up. BJOG. 2000;107(10):1298-301

[12] Martin-Hirsch P, Jarvis G, Kitchener H, Lilford R. Collection devices for obtaining cervical cytology samples. Cochrane Database Syst Rev 2000; :CD001036

[13] Katki HA, Schiffman M, Castle PE, et al. Benchmarking CIN 3+ risk as the basis for incorporating HPV and Pap cotesting into cervical screening and management guidelines. J Low Genit Tract Dis 2013; 17:S28

[14] Paolo Giorgi Rossi, Alessandro Ricciardi, Catherine Cohet,. “Epidemiology and costs of cervical cancer screening and cervical.” BMC Public Health,, 2009: 9:71
[15] Seung-Hyuk Shim, Hyeongsu Kim , In-Sook Sohn , Han-Sung Hwang,. "Nationwide cervical cancer screening in Korea: data from the National Health Insurance Service Cancer Screening Program and National Cancer Screening Program, 2009–2014." J Gynecol Oncol, 2017 Sep;: 28(5):e63
[16] Bayan Maraqa, Isam Lataifeh, Lian Otay, Osama Badran, Yasar Qutaiba. “Prevalence of Abnormal Pap Smears: A Descriptive Study from.” Asian Pacific Journal of Cancer Prevention, Vol 18, 2017: 3117-3121
[17] Addis I, Kenneth D, Berek J. Intraepithelial disease of the cervix, vagina and vulva. In: Berek J, editor. Novak’s Gynecology. 16th ed. Philadelphia: Lippincott Williams and Wilkins; 2007. p. 561-85
[18] İlknur Çeti naslan TÜRKMEN1, Alp USUBÜTÜN2, Aslı ÇAKIR1, Özlem AydIn3, Filiz Aka Bolat 4,. "What does the Data of 354,725 Patients from Turkey Tell." (Turk Patoloji Derg 2017, 33:134-143), 2017: 134-143
[19] Akbari, F Almassi Nokiani.H. "Prevalence of invasive and pre- invasive cervical lesions in Kermanshah." JQUMS, Vol.13, No.1, Spring 2009, 2009: 42-48
[20] Maleki A, Ahmadnia E, Avazeh A, Mazloomzadeh S, Molaei B, Jalilvand A. Prevalence of abnormal papanicolaou test results and related factors among women living in Zanjan, Iran. Asian pacific journal of cancer prevention. Vol 16. 2015
[21] Asnafi N, Shafaei SH, Abdalmaleki SH. "Investigation of abnormal histology and cytology of cervix." jornal of babol university of medical science, 2004: 21-25.
[22] Clement A, Kayode A, Omoladon O, Omoniyi G.O, Onwundiegu U.Age and pattern of pap smears abnormalities : Implications for cervical cancer control in a developing country. JCYTOL, 2017 Oct-Dec; 34(4): 208-211
[23] urmila banik, et all. "pattern of epithelial cell abnormality in pap smear." cytojournal, 2011: 25-30
[24] masoumi sz, et all. "the prevalence of abnormal pap smears in females referred to health centers." journal of education and community health, 2016.16-22
[25] Allame T, et all. "the prevalence of abnormal pap smear results in women attending to esfahan clinics." journal of esfahan medicine college, 2012: 28-31
[26] Arab badkoube kh, et all. "the relevance ofthe results of the pap smear test to the pathology results." journal of nursing and midwifery, 2018: 8-15
[27] Diogo Do Nascimento Franco1, Adriana Cunha Vargas Tomáz1, Angela Andréia. "Screening Cervical Cancer by the Pap Test – Relevance of." Screening Cervical Cancer and Age Ranges, APJCP.2017.18.9.2431: 2431-2435
[28] Ioana pavaleanu et all. Preliminary result of the first cervical cancer screening programme in the north eastern reagion of romania. Journal of medical screening. 2018
[29] pankaj s, et all. "comparison of conventional pap smear and liquid based cytology." indian j cancer, 2018: 50-56
[30] Ann T. Moriarty, MD, MD Amy C. Clayton, SCT(ASCP) Sue Zaleski, MD Michael R. Henry, and MD Mary R. Schwartz. "Unsatisfactory Reporting Rates." Arch Pathol Lab Med—Vol 133, 2009: 1912-1916
[31] Hodgson W, Kaplan KJ, Rodriguez M, McHale MT, Rose GS, Elkas JC. The impact of converting to liquid-based cervical cytology in a military population. Gynecol Oncol. 2005; 99(2):422-6
[32] yousefi z, et all. "the prevalence of unsatisfactory cervical cytology in liquid base method comparison to conventional method." journal of gorgan university of medical science, 2006: 12-16
[33] Nayar R, Wilbur DC. The Pap Test and Bethesda 2014: "The reports of my demise have been greatly exaggerated. (after a quotation from Mark Twain)". J Low Genit Tract Dis 2015; 19:175
[34] Harkness CB, Theofrastous JP, Ibrahim SN, Galvin SL, Lawrence HC. Papanicolaou and thin-layer cervical cytology with colposcopic biopsy control. A comparison. J Reprod Med. 2003;48(9):681-6
[35] Tuncer ZS, Başaran M, Sezgin Y, Firat P, Mocan Kuzey G.Clinical results of a split sample liquid-based cytology (ThinPrep) study of 4,322 patients in a Turkish institution. Eur J Gynaecol Oncol. 2005;26(6):646-8
[36] Hoda rs, et all. "gynecologic cytology on conventional and liquid based preparations." diagn cytopathol, 2013: 152-155
[37] Basu P, et all. "secondary prevention of cervical cancer." Best pract res clin obstet gynaecol, 2018: 70-75