Annals of Medical Research
DOI: 10.5455/annalsmedres.2018.09.179 2019;26(3):322-8

Original Article

Inter-observer compliance in the SurePath liquid-based cervicovaginal smears diagnosed with epithelial cell abnormality

Vahide Baz[1], Selver Ozekinci[2], Gulcin Harman Kamali[2], Selma Sengiz Erhan[2]

[1]Malatya Education and Research Hospital, Medical Pathology, Malatya, Turkey
[2]Health Sciences University Okmeydani Education And Research Hospital, Medical Pathology, Istanbul, Turkey

Abstract

Aim: To assess compliance among observers in the investigation of the liquid-based cervicovaginal smears that were reported epithelial cell abnormality in the Okmeydanı ERH Pathology laboratory.

Material and Methods: 5,250 SurePath liquid-based cervicovaginal smears, which were sent by the pathology laboratory during the period of 5 months, were scanned. One-hundred and twenty-seven smears diagnosed with the epithelial cell abnormality were included in the study, and were reexamined by three pathologists. The Bethesda2001 system was used for evaluation. One of the experts had more experience in SurePath liquid-based cytology than the experience of the others.

Results: There were significant differences between the three physicians because of the Friedman test (p = 0.000) that was applied for the comparison of the reports in 127 smears examined by three experienced experts in SurePath liquid-based cytology. In binary comparison with the Wilcoxon test that was applied to find out the differences among expert pathologists, there was no significant difference between the reports of the two expert pathologists (p = 0.366); however, it was found that there was a significant difference between the pathologist who had more experience and other specialist pathologists (p = 0.000).

Conclusion: Moderate compliance was determined between pathologists 1 and 2, and low-level compliance was determined between pathologists 1-2 and 3.

Keywords: Surepathliquid-Based Cytology; PAP Smear; Inter-Observercompliance.

INTRODUCTION

Every year, over 470,000 new cases of cervical cancer with 233,400 deaths are seen in the world. The high incidence of cervical cancer is a major problem, especially in developing countries (1).

According to 2008 data, 1,443 women were diagnosed with cervical cancer; and it is estimated that 556 women died from cervical cancer in Turkey. In developing countries, cervical cancer is the second most common cancer-related death in the early twenty-first century (2). Cervical cancer differs from person to person after passing from specific precancerous stages in terms of ethiopathogenesis; and becomes an invasive lesion after 13-15 years (3). Early detection of cervical precancerous lesions is of great importance in the prevention of cancer (4).

The detection and treatment of cervical cancer in the precancerous stage will reduce the incidence and mortality. The aim of the cervical cancer screening methods is to catch early cervical intraepithelial neoplasms, to follow the incidence of invasive cancer, to detect the differences between the observers and to test the generalizability of the results. Thus, the patients at risk can give faster results and provide treatment.

For more accurate diagnosis, SurePath liquid-based cervicovaginal cytology (LBC) is more useful than PAP smear. Because the cell details can be more clearly monitored. Therefore, experienced people should evaluate PAP smears particularly.

It is imperative that prior to planning their treatment, pathologists working in laboratory should grade the

Received: 10.09.2018 **Accepted:** 10.12.2018 **Available online:** 20.12.2018
Corresponding Author: Vahide Baz, Malatya Education and Research Hospital, Medical Pathology Malatya, Turkey
E-mail: vahidevurdu@gmail.com

category of epithelial cell abnormality and the disease course according to the results of screening tests of such common and fatal disease to improve the quality of life of the patients. We aimed to evaluate the harmony between pathologists with smear scarring and to increase our compliance rates for better results. In addition, it was observed that it was effective to evaluate the harmony between smear-examining pathologists and to assist the patients based on the diagnoses.

MATERIAL and METHODS

The present study was found to be ethical with the decision of Okmeydanı Education and Research Hospital Ethics Committee on September 23, 2014 with the number 222 (Number: 48670771-514.10-2185). The results of SurePath liquid-based cervicovaginal cytology of all 5,250 patients over 18 years of age who were studied in the pathology laboratory between April 1, 2014 and August 31, 2014 were evaluated. The liquid-based cervicovaginal cytology results of 5250 patients all of whom were over the age of 18 were re-examined by three pathologists from the report archives; and the results of 127 cases who had epithelial cell abnormality were evaluated in Nikon Eclipse Ni-U 930325 light microscope. Each slide was re-examined in the light microscope within an interval of 1 day for at least 10 minutes. During the examinations, only morphological assessments were performed. Regardless of age and sex of the cases, reports were done according to the Bethesda reporting system, and the results were recorded.

Pathology specialists participating in the study were coded with numbers 1, 2, and 3; and the one who was coded as 2 had equal experience with SurePath liquid-based cervicovaginal cytology, and particular experience of number 3 was greater.

Our study was designed in such a way in which a mean of 0.5 difference could be differentiated with a standard deviation of 1.3 with a=0.05 and b=0.20 error margins in at least 107 cases with G Power software and SPSS 17.0 package program.

SurePath liquid-based cytology results are expressed as ordinal variables; Atypical squamous cells cannot exclude HSIL (ASC-H) =4, High-grade squamous intraepithelial lesion (HSIL) = 5, the Friedman test was performed to determine whether there was a significant difference between the three pathological SurePath liquid-based cervicovaginal cytology results. If a significant difference was found because of the Friedman test, the Wilcoxon test was performed in duplicate to determine which specialists had the difference between the results.

In addition, the Kappa test was performed in duplicate to compare the compliance of the specialists with the results, and the compliance was compared according to the Kappa values.

By the Multinomial Logistic Regression method, the results of the third specialist were compared.

We assessed whether or not there was a statistically significant difference between the three pathological SurePath liquid-based cytology results.

RESULTS

One-hundred-twenty-seven cases were included in the study, and the ages of the participants were between 18 and 77 with an average age of 42.12 years (Table 1). Age distribution according to age groups is given in Table 2.

Table 1. Averages and extremities

	Case Age
Average	42.12
Standard deviation	11.965
Minimum	18
Maximum	77

Table 2. Distribution of age groups

Age Groups	Number	Percent	Cumulative Percentage
18-29	15	11.8	11.8
30-39	39	30.7	42.5
40-49	44	34.6	77.2
50-77	29	22.8	100
Total	127	100	

A comparison of the results of SurePath liquid-based cervicovaginal cytology examinations of 127 patients with the Friedman test revealed that there was a statistically significant difference between the three pathologists (p = 0.000*).

In binary comparisons with Wilcoxon test, there was no statistically significant difference between the results of pathologist 1 and 2 (p = 0.366) (Table 3). It is also shown in Table 3 that there was a statistically significant difference between pathologist 1 and 3 (p = 0.000*) and pathologist 2 and 3 (p = 0.000*).

Table 3.Binary comparison results among pathologists

	Kappa	p
Pathologist1 - pathologist2	0.472	0.366
Pathologist1 - pathologist3	0.124	0.000
Pathologist2 - pathologist3	0.179	0.000

The kappa value of pathologist 1 and 2 was statistically significant and different from 0 (p = 0.000*) in the Kappa test that was carried out to find the correspondence between the three pathologists, two-in-one pairs; and the results were found to be moderately consistent with the exception of 0.472 kappa values.

In Table 4, the general compliance between pathologist 1 and 2 is given as 81 (47 + 11 + 13 + 0 + 10) / 127 = 63%. The value of kappa between pathologist 1 and 3 was statistically significant and different from zero (p = 0.003*), and 0.124 values were found to be at a low level of compliance between the results of them.

The general compliance between pathologist 1 and 3 was found to be 39 (12 + 3 + 11 + 0 + 13) / 127 = 30% as given in Table 5.

The value of kappa between pathologist 2 and 3 was statistically significant and was different from zero (p = 0.000*). The kappa value was 0.179, which means there was a low level of compliance.

Table 6 shows that the general compliance between pathologist 2 and 3 was 45 (13 + 6 + 14 + 1 + 11) / 127 = 35%.

Table 4. Pathologist 1 and pathologist 2 cross table

			Pathologist 2					
			Reactive	ASC-US	LSIL	ASC-H	HSIL	Total
Pathologist 1	Reactive	Number (n)	47	10	2	1	2	62
		%Pathologist 1	75.8	16.1	3.2	1.6	3.2	100
		% Pathologist 2	79.7	35.7	8.3	50	14.3	48
	ASC-US	Number	7	11	3	1	0	22
		% Pathologist 1	31.8	50	13.6	4.5	0	100
		% Pathologist 2	11.9	39.3	12.5	50	0	17.3
	LSIL	Number	2	6	13	0	1	22
		% Pathologist 1	9.1	27.3	59.1	0	4.5	100
		% Pathologist 2	3.4	21.4	54.2	0	7.1	17.3
	ASC-H	Number	1	0	0	0	1	2
		% Pathologist 1	50	0	0	0	50	100
		% Pathologist 2	1.7	0	0	0	7.1	1.6
	HSIL	Number	2	1	6	0	10	19
		% Pathologist 1	10.5	5.3	31.6	0	52.6	100
		% Pathologist 2	3.4	3.6	25	0	71.4	15
	Total	Number	59	28	24	2	14	127
		% Pathologist 1	46.5	22	18.9	1.6	11	100
		% Pathologist 2	100	100	100	100	100	100

Table 5. Pathologist 1 and pathologist 3 cross table

			Pathologist 3					
			Reactive	ASC-US	LSIL	ASC-H	HSIL	Total
Pathologist 1	Reactive	Number (n)	12	17	29	2	2	62
		% Pathologist 1	19.4	27.4	46.8	3.2	3.2	100
		% Pathologist 3	63.2	77.3	50.9	33.3	8.7	48
	ASC-US	Number (n)	3	3	11	1	4	22
		% Pathologist 1	13.6	13.6	50.0	4.5	18.2	100.
		% Pathologist 3	15.8	13.6	19.3	16.7	17.4	17.3
	LSIL	Number (n)	4	2	11	2	3	22
		% Pathologist 1	18.2	9.1	50.0	9.1	13.6	100
		% Pathologist 3	21.1	9.1	19.3	33.3	13.0	17.3
	ASC-H	Number(n)	0	0	1	0	1	2
		% Pathologist1	0	0	50.0	0	50	100
		% Pathologist 3	0	0	1.8	0	4.3	1.6
	HSIL	Number (n)	0	0	5	1	13	19
		% Pathologist 1	0	0	26.3	5.3	68.4	100
		%Pathologist 3	0	0	8.8	16.7	56.5	15
	Total	Number (n)	19	22	57	6	23	127
		% Pathologist 1	15	17.3	44.9	4.7	18.1	100
		% Pathologist 3	100	100	100	100	100	100

Table 6. Pathologist 2 and pathologist 3 cross table

			Pathologist 3					
			Reactive	ASC-US	LSIL	ASC-H	HSIL	Total
Pathologist 2	Reactive	Number	13	15	25	1	5	59
		% Pathologist 2	22	25.4	42.4	1.7	8.5	100
		% Pathologist 3	68.4	68.2	43.9	16.7	21.7	46.5
	ASC-US	Number	3	6	16	1	2	28
		% Pathologist 2	10.7	21.4	57.1	3.6	7.1	100
		% Pathologist 3	15.8	27.3	28.1	16.7	8.7	22
	LSIL	Number	3	0	14	3	4	24
		% Pathologist 2	12.5	0	58.3	12.5	16.7	100
		% Pathologist 3	15.8	0	24.6	50	17.4	18.9
	ASC-H	Number	0	0	0	1	1	2
		% Pathologist 2	0	0	0	50	50	100
		% Pathologist 3	0	0	0	16.7	4.3	1.6
	HSIL	Number	0	1	2	0	11	14
		% Pathologist 2	0	7.1	14.3	0	78.6	100
		% Pathologist 3	0	4.5	3.5	0	47.8	11
	Total	Number	19	22	57	6	23	127
		% Pathologist 2	15	17.3	44.9	4.7	18.1	100
		% Pathologist 3	100	100	100	100	100	100

There was no statistically significant difference among three pathologists (p = 0.139) as a result of the Friedman test in comparison with SurePath liquid-based cervicovaginal cytology reports for 18-29-year-old cases.

There was a statistically significant difference between three pathologists (p= 0.000*) as a result of the Friedman test in comparison with SurePath liquid-based cervicovaginal cytology reports of the 30-39 age group.

In binary comparisons with Wilcoxon test, no statistically significant difference was found between pathologist 1 and 3 (p = 0.000*) and between pathologist 2 and 3 (p = 0.000*).

The Friedman test in comparison with SurePath liquid-based cervicovaginal cytology reports for 40-49-year-old subjects showed that there was a significant difference between the three pathologists (p = 0.000*).

In binary comparisons with Wilcoxon test, there was no statistically significant difference between the reports of pathologist 1 and 2 (p = 0.164). There was a statistically significant difference between pathologist 1 and 3 (p= 0.008*) and between pathologist 2 and 3 (p = 0.000*).

The Friedman test in comparison with SurePath liquid-based cervicovaginal cytology reports for 50-77-year-old subjects showed a significant difference between the three pathologists (p = 0.000*).

In binary comparisons with Wilcoxon test, there was no statistically significant difference between pathologist 1 and 2 (p = 0.695). There was a statistical difference between pathologist 2 and 3 (p = 0.005*) (p = 0.000).

DISCUSSION

Cervical cancer is a health problem all over the world. The prevalence of it is 12% among the cancers seen in women all over the world. Precancerous lesions are often seen under 40 years of age (5,6).

In our study, the microscope slides of 127 cases with epithelial cell abnormality from a sample of SurePath liquid-based cervicovaginal cytology of 5.250 cases were examined again. Among these, 2.42% of the cases were reported as epithelial cell abnormality. According to the literature data, this ratio in relation to epithelial cell abnormality is less. This may be because the number of cases participating in the study was low.

The mean age for LSIL (Low-grade squamous intraepithelial lesion) and HSIL was 34.7 and 37.7 years. It is important to start screening programs before age 40 (7). The average age of 127 patients in our study was 42.12. The mean age for LSIL is 40.73, while for HSIL, it is 46.77. Our study was small-scale, the average age of our cases was big, and our findings showed differences from the literature.

In the literature, ASC-US (Atypical squamous cells of unknown importance) has been reported to be seen under the age of 40 years (7). It was reported that ASC-US was seen in premenopausal women; LSIL was seen in both premenopausal and postmenopausal women; and HSIL was seen in postmenopausal women (8). The average age in our study was 42.12. The total number of ASC-US of the three pathologists was 53. Among these, 24 cases age was under 40 years old. The other 29 was over 40 years old. When we considered the age averages, it was consistent with the literature.

In a study of ASC-H with a 20-minute Thin prep, Kappa = 0.11 was noted among the observers; and it was reported that there was a low degree of compliance (9). In our study, ASC-H was statistically analyzed between pathologist 1 and 2; and there was a low degree of compliance between pathologist 3 and 1-2.

After using SurePath, the ASC-US / LSIL ratio is reduced. LSIL diagnosis increases with time (10).

In our study, this rate was found to be 1.27 for pathologist 1; 1.0 for 2; and 0.38 for 3. The data of pathologists 1 and 2 were low, which is consistent with the literature, and the data of pathologist 3 were found to be perfectly compatible.

In another study performed with 313 patients with a Pap test, except for squamous cell carcinoma cases, cytologist 1 had a diagnosis of reactive changes in 169 cases (64%), and cytologist 2 in 154 cases (58.77%). A total of 125 patients (47.71%) were diagnosed with reactive mutations (change). Cytologists were good compatible with the diagnosis of reactive disease (11).

In our study, pathologist 1 had a diagnosis as reactive changes in 59 cases (46.5%), and pathologist 2 in 62 cases (48.8%). The common diagnoses were in 47 cases (37%). This result showed a better fit than the literature. The pathologist diagnosed 15% of the reactive changes in only 19 cases out of 127 cases. Pathologist 3 diagnosed reactive changes in 25 cases. According to this result, if comparison was made in literature, pathologist 3 was found to be incompatible with other pathologists and the literature statistically. This result suggested that the diagnoses of pathologists with similar experience are more compatible with each other.

In the study of Sriamporn et al. (11), cytologist 1 diagnosed ASC-US in 59 cases (22.52%) and cytologist 2 in 48 cases (18.2%). They had a common diagnosis in 19 cases. In the diagnoses of cytologist 1 and cytologist 2, there is a statistically significant agreement with regard to ASC-US rates; however, based on the common diagnosis, there is a statistically significant low correlation between them. In the study of Stoler et al. (12), ASC-US remained the same in both groups. In our study, the average of pre-40 ages from 127 cases was 18.2, while the average of post-40 years ages was 31. The average age of ASC-US is 40 before and after age 10. In our study, pathologist 1 had a ASC-US diagnosis rate of 22% with 28 cases, pathologist 2 had a ASC-US diagnosis rate of 17.3% with 22 cases; pathologist 3 had a ASC-US diagnosis rate of %17.3 with 22 cases (Table 7). Compared with the literature, higher compliance and statistically excellent compliance were observed. Pathologist 1 and 2 diagnosed an ASC-US in 11 cases. Pathologist 3 and other pathologists had a common diagnosis in three and six cases, respectively. According to this result, pathologist 3 was in a statistically low level compliance with other pathologists.

In the study of Sriamporn et al. (11) cytologist 1 diagnosed LSIL in 21 cases (8.01%), and cytologist 2 in 20 cases (7.63%). In 10 cases, both cytologists had LSIL diagnosis. According to this result, there was a good level of compliance; however, moderate compliance was observed when the common diagnosis was considered (11). In our study, pathologist 2 had a LSIL diagnosis in 24 cases (18.9%), pathologist 1 in 22 cases (17.3%), and pathologist 3 in 57 cases (44.9%) (Table 7). Pathologist 1 and 2 shared LSIL diagnosis in 13 patients, pathologist 3 and 1 in 11 patients, pathologist 3 and 2 in 14 patients. Statistically, excellent agreement between pathologist 1 and 2 was found to be moderate in terms of common diagnosis. No statistically significant difference was found between pathologist 3 and other pathologists. A good level of adjustment was observed among the three pathologists considering the common diagnosis. Pathologist 3 disagreed due to great number of experiences.

Table 7. Diagnosis of pathologists

	Reactive	ASC-US	LSIL	ASC-H	HSIL
Pathologist 1	62%48.8	22%17.3	22%17.3	2%1.6	19%15
Pathologist 2	59%46.5	28%22	24%18.9	2%1.6	14%11
Pathologist 3	19%15	22%17.3	57%44.9	6%4.7	23%18.1

According to the literature, cytologist 1 did not diagnose ASC-H; however, only in 11 cases (4.2%) it was diagnosed by cytologist 2, so nonconformity was reported (11). In our study, pathologist 1 diagnosed ASC-H in 2 cases (1.6%), pathologist 2 in 2 cases (1.6%), and pathologist 3 in 6 cases (4.72%), respectively (Table 7). Pathologists 1 and 2 and pathologists 1 and 3 have no common diagnoses in terms of ASC-H. There is one common diagnosis between pathologist 2 and 3. Statistically good agreement was observed between pathologist 1 and 2. Our results were consistent with the literature, and no ASC-H compliance was detected among the observers. Pathologists 2 and 3 were observed to be statistically low-matched.

According to the studies in the literature (11), cytologist 1 diagnosed 5.34% HSIL in 14 cases while cytologist 2 diagnosed 11.45% HSIL in 30 cases. A total of 11 cases were both HSIL. The intermediate compliance was found statistically significant in terms of common diagnosis (11). In our study, pathologist 2 reported the diagnosis of HSIL in 14 cases (11%), pathologist 1 in 19 cases (15%), and pathologist 3 in 23 cases (18.1%) (Table 7). Pathologist 1 and 2 had 10 cases of HSIL, pathologist 1 and 3 - 13 cases, pathologists 2 and 3 - 11 cases, respectively. There was a higher degree of compliance among pathologists participating in the statistical study according to the literature. We have seen better harmonization regarding common diagnoses in our study compared to the literature. This was thought to be caused by the morphological diagnosis without regard to history information.

Stoler et al. (12) evaluated 5000 smears in 2001 and classified four as negative, ASC-US, LSIL, HSIL and found a positive smear ratio of 37%. The agreement between the two pathologists was moderate (k= 0.46).

In our study, 52 positive cervical smears were evaluated in

5250 SurePath liquid-based cervicovaginal cytology. This corresponds to 2.42% of all smears. In our study, diagnoses were divided into five diagnostic groups: Reactive, ASC-US, LSIL, ASC-H, and HSIL. Pathologists 1 and 2 were moderately compatible with k = 0.472; however, it was found to be consistent with the literature. It was observed that the correlation between the observers was similar between the single-layered cytological method and the SurePath method in the liquid-based cytology.

In terms of all diagnostic groups, pathologists 1 and 3 were found to be at low level with k = 0.124 and pathologists 2 and 3 with k = 0.179. When we compare it with the literature, it is seen that the last two results are less compatible.

In the study performed by Sanjay et al. (13), ASC-H ratio was increased (n: 11.189) (3.4%) (p <0.001) compared with 40 years of age.

In our study, the mean LSIL areas before and after 40 years of age were 17, while the average of ASC-H areas increased from 1.3 before age 40 to 2 after age 40. The mean of HSIL diagnostic areas also rose from 7.1 to 8.

In the literature, similar rates have been reported in the areas of ASC-US and LSIL before and after 40 years of age. In our study, ASC-H and HSIL after 40 years of age were seen to be in accordance with the literature.

As a result, there was no statistical significant difference between age and grade between pathologists 1 and 2.

In our study, no statistically significant differences were found in the cases who were 50 years or older, in terms of the difference between pathologist 1 and 2. Besides, there was a statistical significant difference not only between pathologist 1 and 3, but also between pathologists 2 and 3. As age increases, the 3-code pathologist assessed with a high degree of epithelial cell abnormality according to the data. It was thought that this result might be due to education differences, experience differences and secondary changes in atrophy.

Pathologists 1 and 2 were identical in 81 out of 127 cases, and generally, the reactive changes were concentrated in the ASC-US and LSIL diagnoses (Table 7). Less compliance was observed with ASC-US and HSIL (Table 7).

The diagnostic consistency between pathologists 1 and 3 is 39 cases, while the different diagnosis is 88 cases. The diagnostic consistency between pathologists 2 and 3 is 45 cases, while different diagnosis is 82 cases. In the study, it was seen that experts 1 and 2 were moderately compatible between themselves. Although there was a low level of agreement among pathologists 3, 1 and 2, a statistical significant difference was observed.

In the 18-29, 40-49, and 50-77 age groups, median values were found to be reactive changes for pathologists 1 and 2 and LSIL for pathologist 3 as ASC-US. The median value of the 30-39 age group was ASC-US for pathologists 1 and 2, while being LSIL for pathologist 3.

Considering all cases in our study, pathologist 3 was found to have a higher grade in the epithelial cell abnormality category in general, than pathologist 1 and 2. Pathologist 1 and 2 could have said to be more or less compatible with each other because their experience levels were partially similar. Pathologist 3 could yield different results as he was more experienced. It can be said that the increase in difference is directly proportional to experiences.

CONCLUSION

SurePath liquid based cervicovaginal cytology (LBC) can be used for diagnosis that is more accurate. This method reduces inflammation in the sample, clearing blood and mucus. In this way, a clearer image is provided and the insufficient sample rate is reduced.

It is imperative that prior to planning their treatment, pathologists working in laboratory should grade the category of epithelial cell abnormality and the disease course according to the results of screening tests of such common and fatal disease to improve the quality of life of the patients. We aimed to evaluate the harmony between pathologists with smear scarring and to increase our compliance rates for better results. In addition, it was observed that it was effective to evaluate the harmony between smear-examining pathologists and to assist the patients based on the diagnoses.

In our study, there is a low level of harmony between pathologist 1, 2 and 3. The best that could be considered is moderate coherence between pathologist 1 and 2.

According to the result of the report, depending on whether the short intermittent follow-up or long intermittent follow-up or surgical intervention results are required, it will yield better results if at least two or three specialists assess the cases if possible.

If LEEP or conization is applied to the patient in the presence of colposcopy, the biopsy should be required for histopathological diagnosis.

DATA AVAILABILITY

All data relevant to this publication are included in the text and hence are available to everyone.

Competing interests: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports
Ethical approval: The present study was found to be ethic in accordance with Okmeydani Education and Research Hospital Ethics Committee's decision dated 23.09.2014 and numbered 222 (Number: 48670771-514.10-2185).

Vahide Baz ORCID: 0000-0002-5655-5182
Selver Ozekinci ORCID: 0000-0002-0645-8755
Gulcin Harman Kamali ORCID: 0000-0003-4135-0165
Selma Sengiz Erhan ORCID: 0000-0001-8810-8806

REFERENCES

1. Akyüz A, Güvenç G, Yavan T. ve ark. Kadınların Pap smear yaptırma durumları ile bunu etkileyen faktörlerin belirlenmesi. Gülhane Tıp Dergisi 2006;48:25-9.
2. Parkin DM. "New cases in 2000". Lancet Oncol 2001;2:533-43.
3. Atasü T, Aydınlı K. Jinekoloji ve Obstetrik pratiğinde kolposkopi, jinekolojik Onkoloji 1996;12:182.

4. Özbay K, Yardım T. Servikal lezyonların değerlendirilmesinde kolposkopi ve PAP smearların etkinliklerinin araştırılması. Jinekoloji ve Obstetrik Dergisi 2005;19:228-32.
5. Ferlay J, Bray F, Pisani P. Globocon 2000: Cancer incidence, mortality and prevalence worldwide. Version 1.0 IARC Cancer Base No. 5 Lyon: IARC Press; 2001.
6. Holowaty P, Miller AB, Rohan T, et al. Natural history of dysplasia of uterine cervix. JNCI 1999;91:252-8.
7. Boman F, Duhamel A, Trench QD, et al. Evaluation of cytological screening for cancers and precancerous lesions of the cervix. Bull Cancer 2003;90:643-7.
8. Rader AE, Rose PG, Rodriguez M, et al. Atypical squamous cells of undetermined significance in women over 55. Comparison with general population and implications for management. Acta Cytol 1999;43:357-62.
9. Quddus MR, Sung CJ, Steinhoff MM, et al. Atypical squamous metaplastic cells: Reproducibility, outcome and diagnostic features on ThinPrep Pap test. Cancer 2001;93:16-22.
10. Maurice Fremont-Smith, James Marino, Bryan Griffin et al. Comparison of the SurePathTM Liquid-Based Papanicolaou Smear with the Conventional Papanicolaou Smear in a Multisite Direct to Vial Study 2004;102:269-79.
11. Supannee Sriamporn, Onanong Kritpetcharat, Pekka Nieminen, et al. Consistency of Cytology Diagnosis for Cervical Cancer between Two Laboratories 2005;6:208-12.
12. Stoler MH, Schiffman M (2001). Atypical Squamous Cells of Undetermined Significance-Low-grade Squamous Intraepithelial Lesion Triage Study (ALTS) Group. Interobserver reproducibility of cervical cytologic and histologic interpretations: Realistic estimates from the ASCUS-LSIL Triage Study. JAMA, 285, 1500-5.
13. Sanjay Gupta, Pushpa Sodhani Sarita Sardana, Kaushik Halder, Veena Singh, Krishan Lal Chachra, Ashok Sehgal. Spectrum of epithelial cell abnormalities of uterine cervix in a cervical cancer screening programme: Implications for resource limited settings 2007:134 Suppl 238-42.