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The Evaluation of Cervical Cytology Results in a Tertiary Health Centre Between 2006-2015

Üçüncü Basamak Bir Sağlık Kuruluşunda 2006-2015 Yılları Arasındaki Servikal Sitoloji Sonuçlarının Değerlendirilmesi

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Abstract
Objectives: The main goal of cervical cancer cytologic screening is to prevent mortality and morbidity associated with cervical cancer. We aimed to retrospectively evaluate the prevalence of cervical cytological abnormalities in patient records obtained from electronic data at our tertiary hospital.
Materials and Methods: Demographic characteristics and data on cervical cytological abnormalities were evaluated from patients (n=54999) who underwent Pap tests in our hospital from 2006 to 2015.
Results: Data were collected from 54999 patients. Overall, the prevalence of cervical cytological abnormalities was 2.27%; the prevalence of ASCUS, LSIL, and HSIL was 1.29%, 0.27% and 0.11%, respectively. The highest prevalence of HSIL was seen in the group older than 71 years.
Conclusion: The abnormal cervical cytological prevalence rate in Turkey is similar to Europe, Israel, and North America. The data from our hospital over 10 years are compatible with data from various centres around the world and the country, apart from the increase in the incidence of abnormal smears in older age groups.
Key words: Abnormal cervical cytology, cancer screening, cervical precanserous lesions, Pap smear

Öz
Amaç: Servikal kanser taramasının amacı, servikal kanser ile ilişkili morbidite ve mortaliteyi azaltmaktır. Araştırmamızda hastanemizin elektronik kayıtları retrospektif olarak incelenerek servikal sitolojik anomalilerin sıklığının değerlendirilmesi amaçlanmıştır.
Materyal ve Metot: Hastane elektronik kayıtlarından 2006-2015 yılları arasında 54999 hastanın demografik verisine ve Pap-smear sonuçlarına ulaşılmıştır.
Bulgular: Servikal sitolojik anomalilerin sıklığı %2,27; ASCUS, LSIL, HSIL sıklığı sırasıyla; %1,29; %0,27; % 0,11 olduğu görüldü. Hastalarda HSIL sıklığının en fazla olduğu yaş grubunun 71 yaş ve üzeri grup olduğu görüldü.
Sonuç: Türkiye'deki anormal servikal sitoloji sıklığı Avrupa, israil ve Kuzey Amerika ile benzer bulunmuştur. Hastanemizin 10 yılı aşkın süredeki servikal sitoloji sonuçları dünyanın birçok ülkesi ile uyumlu olsa da ileri yaş grubunda artmış anormal smear sonuçlarına rastlanmıştır.
Anahtar kelimeler: Anormal servikal sitoloji, kanser taraması, Pap- smear, servikal prekanseröz lezyonlar

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Introduction

Cervical cancer is 7th place with 3.7% incidence among cancers all over the world. It is 4th place in women after breast, colon and lung cancer. Approximately 528.000 new

cases are estimated each year.[1] While cervical cancer was the most common cause of cancer deaths among female cancers in the mid-20th century, it is ranked 14th in cancer deaths in the United States today.[2] This reduction has been achieved by ensuring early diagnosis with screening tests and an increase in survival and identification of preinvasive lesions.[2,3]

The main goal of cervical cancer screening is to prevent mortality and morbidity associated with cervical cancer. The optimal screening method should show preinvasive lesions which will turn into cervical cancer, and it should also prevent unnecessary treatment for non-cancerous benign lesions. Although false-positive rates are high with the Pap smear test, it reduces the incidence of cancer in countries where screening is used effectively.[4] The Pap smear test (cytological screening) has been used as a standard screening test since 1941 to screen cervical cancer and precancerous lesions. After the relationship between persistent human papilloma virus (HPV) infection and cervical cancer was revealed, HPV began to be tested with cytology screening.

The age to begin screening, screening intervals and age to cease screening are important in screening guidelines. Cytological screening is not recommended before the age of 21 years regardless of the age of initial sexual activity in women. The screening can be stopped at 65 years in patients who have previous negative screening results and no CIN 2 or highergrade lesion in the last 20 years.[4] Cytological screening is recommended at intervals of 3 years in patients with a negative scan result. Immunosuppressed patients, patients with exposure to diethylstilbestrol (DES) and patients with hysterectomy are assessed separately in the screening guidelines.[4,5]

The Pap smear test is cytological screening and it is also performed by examining cells which contain the transformation zone where cervical cancer develops. In randomised controlled studies, it was shown that conventional and liquid-based studies were not superior to each other in defining precancerous lesions.[6-8] HPV may be examined in samples taken for liquid-based examination and this may be an advantage of the liquid-based test.

We aimed to investigate the distribution of cytological screening results according to years and ages between 2006 and 2015 in our tertiary health centre. Based on the data that we obtained, we summarise the adequacy of our screening program for the prevention of cervical cancer.

Materials and Methods

In this retrospective study, the results of 54999 Pap smears which were taken in the gynaecology outpatient clinic of our hospital between 2006 and 2015 were examined. The data were electronically obtained from electronic data at our tertiary hospital. The age and smear results of the patients were evaluated along with the year when the smear was taken.

The Pap smear tests assessed in our study were studied by conventional methods and the 2001 Bethesda system is used in the evaluation of the results.[9] In our study, the results reported as inflammation and data from patients without the transformation zone were grouped separately. The patients with NILM and patients with abnormal squamous and glandular cells were grouped separately. The cuff smear results of

patients with hysterectomy were excluded from the study, the patients were divided into 10-year age groups including patients under the age of 21 and the patients over 70 years as separate groups while evaluating the obtained data. Also 10-year data were grouped as the first 5 years and the last 5 years. This study was approved by the Clinical Research Ethics Committee of Yıldırım Beyazıt University (Number: 26379996/18)

Statistics

The number (n) and percentage (%) are given to show the distribution of demographic data such as the age groups, diagnosis and Pap smear results of individuals participating in the study.

The Pap smear results according to the years are given as number (n) and their rates in that year are given as a percentage (%). The number (n) and percentage (%) were used to represent the age groups and the Pap smear results. Graphical representations were created for all groups.

Because of the Pap smear screening of individuals according to years, cross tables were created to show the distribution of abnormal squamous cells and abnormal glandular cells of patients with negative Pap test and the chi-square test for linear trend was completed with the number (n) and percentage (%) values.

IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and MS-Excel 2007 programs were used for statistical analysis and calculations. The statistical significance level was accepted as $p<0.05$.

Table 1. Demographic analysis of data

	n (%)
Age groups (years)	241 (0.43)
<21	26563 (48.29)
21-45	26551 (48.27)
46-70	1644 (2.98)
≥71	
Number of patients by 5 years	25231 (45.87)
2006-2010	29768 (54.12)
2011-2015	
Results of cytology	53750 (97.72)
NILM*	938(1.70)
Abnormal squamous cell	311 (0.56)

*NILM: Negative for Intraepithelial Lesion and Malignite

Results

The results of 54999 patients were evaluated retrospectively. Of the individuals participating in the study, 0.43% (n=241) were under the age of 21, 48.29% (n=26563) were between the ages of 21-45 and 48.27% (n=26551) were between the ages of 46-70. Moreover, 2.98% (n=1644) were 71 years and older (Table 1). While the results of 97.72% (n=53750) of all screened women were reported as negative for intraepithelial lesion or malignancy, the results of 1.70% (n=938) were reported as abnormal squamous cells and the results of 0.56% (n=311) were reported as abnormal glandular cells. When we examined the results according to year, patients reached maximum numbers (n=6613, 12.02%) in 2013 and minimum numbers (n=1602, 2.91%) in 2006.

When the distribution of all results according to year is examined, while the total number of patients continued to increase until 2011, it decreased in 2012 but the number of patients who had abnormal glandular cells on the Pap smear test increased. The total number of patients increased again in 2013 and the smear results which contained abnormal squamous and glandular cells increased along with it. The number of individuals diagnosed with abnormal squamous cells increased 168.25% in 2007 compared to 2006, along with an increase in the total number of patients. Moreover, the number of individuals diagnosed with abnormal glandular cells increased by 288.88%. The distribution of the Pap smear results according to the years is summarised in Table 2. The distribution of smear results according to age groups is given in Table 3.

Table 2. The distribution of cytology results by year

	2006 n(%)	**2007 n(%)**	**2008 n(%)**	**2009 n(%)**	**2010 n(%)**	**2011 n(%)**	**2012 n(%)**	**2013 n(%)**	**2014 n(%)**	**2015 n(%)**
NILM	1521 (94.94)	5088 (95.51)	5666 (98.44)	6215 (98.14)	6091 (98.04)	6511 (98.53)	5365 (98.17)	6465 (97.46)	5614 (97.80)	5214 (97.60)
ASC	63 (3.93)	169 (3.17)	44 (0.76)	92 (1.45)	97 (1.56)	78 (1.18)	74 (1.35)	113 (1.71)	95 (0.66)	113 (2.12)
AGC	18 (1.13)	70 (1.31)	46 (0.80)	26 (0.41)	25 (0.40)	19 (0.29)	26 (0.48)	35 (0.53)	31 (0.54)	15 (0.28)
Total	1602 (100)	5327 (100)	5756 (100)	6333 (100)	6213 (100)	6608 (100)	5465 (100)	6613 (100)	5740 (100)	5342 (100)

NILM: Negative for Intraepithelial Lesion and Malignite, ASC: Abnormal squamous cell, AGC: Abnormal glanduler cell

When trend analysis was completed (Table 4), the ratio of abnormal epithelium (squamous) cells on the Pap smear test was significantly higher in 2006 compared to the other years ($p<0.05$). The smear results which contained abnormal glandular cells were significantly higher in 2011 compared to the other years ($p<0.05$).

When abnormal results are individually assessed, the most common abnormal smear results in our study were ASC-US (1.29%) and it was observed most often between the

ages of 21-45 (1.32%). The rate of LSIL was found to be 0.27% in our study's patient population. In the distribution according to age, the rate of LSIL was highest in the group under 21 years of age (0.42%). HSIL from high-grade lesions was found to be 0,11% in our study's patient population and it was highest in the group over 71 years of age. The total number of smear results was reported as 25 in the ASC-H group in which high-grade lesions cannot be excluded and frequency could not be reported as %. The rate of smear results which contained abnormal glandular cells was found to be 0.61%.

Table 3. The distribution of cytology results by age

	<21 years n (%)	**21-45 years n (%)**	**46-70 years n (%)**	**+71 years n (%)**
NILM	240(99.58)	26004(97.89)	25909(97.58)	1597(97.14)
ASC	1(0.4)	463(1.74)	447(1.68)	27(1.64)
AGC	0(0)	96(0.36)	195(0.73)	20(1.21)
Total	241(100)	26563(100)	26551(100)	1644(100)

NILM: Negative for Intraepithelial Lesion and Malignite, ASC: Abnormal squamous cell, AGC: Abnormal glanduler cell

Table 4. Trend analysis of squamous cell abnormality by years

Years	**NILM**	**Abnormal Squamous cell**	**Statistical anlaysis***	
	n (%)	**n (%)**	χ^2	**p**
2006	1521 (96.02)	63 (3.93)	8.569	0.003
2007	5088 (96.78)	169 (3.21)		
2008	5666 (99.22)	44 (0.77)		
2009	6215 (98.54)	92 (1.45)		
2010	6091 (98.43)	97 (1.56)		
2011	6511 (98.81)	78 (1.18)		
2012	5365 (98.63)	74 (1.36)		
2013	6465 (98.28)	113 (1.71)		
2014	5614 (98.33)	95 (1.66)		
2015	5214 (97.87)	113 (2.12)		

NILM: Negative for Intraepithelial Lesion and Malignite

Discussion

In our study, we aimed to investigate the distribution of Pap smear results according to year and age within 10 years between 2006 and 2015 in our tertiary health centre and determine whether there was any change in the smear results of different age groups over the years. The rate of abnormal smear results in all patients was found to be 2.27%. In previous studies, abnormal smear rate varies according to data from various

countries and it also starts from 0.3% and is up to 17.3-43.2% in South Africa.[10-14] According to data from studies conducted in 2009 and 2010 in our country, abnormal smear results were reported as 1.8% and 1.2%, respectively.[15,16] The first of these studies[15] examined 140 thousand smear results in 33 centres across the country and included 1-year data. Another study[16] included only married women and so it was considered that the rate was higher in our study. Abnormal smear results reached the maximum number in 2006 (5.06%) and the minimum number in 2011 (1.47%). Abnormal smear results decreased between 2006 (opening of our hospital) and 2011, but they were found to increase again after 2011. The rate of abnormal results was found to be 2.40% in 2015. While abnormal smear results were observed most often in the group over 71 years of age (2.81%), they were observed least in the group under 21 years of age (0.43%). The greater incidence of abnormal smear results in older age groups can be explained by taking smears if there is clinical suspicion in the patients in this group. In recent times, if there are no appropriate negative smear results in accordance with the recommendations in the guidelines smear is taken in patients in this age group.

The most common abnormal smear result in our study was ASC-US and the rate was 1.29% observed in all patients. The rate of AS-CUS was reported as 1.07% in a major study in Turkey.[15] In another study, 29295 Pap smear results were examined and the rate of ASC-US was reported as 9.9%.[17] In another study which examined 711000 Pap smear results from Israel, it was specified as 2.72%.[10] In our study, ASC-US was observed most often between the ages of 21-45 (1.32%). ASC-US was observed most often at the age of 42 in this age group (4.21%). In other studies, it was stated that ASC-US was observed most often at 37.8 years[21] and at 41.2 years.[11] It was most frequently identified in 2006 according to the annual distribution (2.63%). The rate of ASC-US varied over the years. In other studies, it was shown that the largest increase was for ASC-US results among abnormal smear results over the years.[10,18]

The rate of LSIL was found to be 0.27% in our study's patient population. In the distribution according to age, LSIL was observed most often under 21 years of age (0.42%). Although the rate of LSIL varies in different countries of the world, there are studies showing that its rate is between 2.5-6.3%.[17,19] It was given as 0.07% in a multicentre study in Turkey.[15] When the rate according to age group is examined, LSIL was observed most often in the adolescent period (between 13-22 years) in one study and between the ages of 15-30 in another study.[20] The result of our study is consistent with studies showing an increased proportion among younger age groups. It is an expected result due to HPV transmission in these patients that engage in sexual intercourse at an early age and do not have enough information about sexual health and contraception. When assessed separately according to age, LSIL was seen most frequently in 33-year-old women, and LSIL was seen most frequently at 33.24 years in one study conducted on this subject [10], at 41.5 years in data from Iran[11] and at 32.3 years in a study performed in India.[12] When examined over the years, LSIL was observed most often in 2011 and was seen at 1.19%. The rate of LSIL varied over the years.

HSIL from high-grade lesions was found to be 0,11% in our study's patient population. In other studies, the rate of HSIL has been given as 0.34-1.18%.[10,19] HSIL was observed less frequently in our country compared to the numbers in the literature. The incidence of HSIL was found to be 0,17 in a multicentre study.[15] HSIL was observed

most often in the group over 71 years of age in our study. In other studies, HSIL was observed most often between the ages of 25-34[10] and between the ages of 25-45.[19] HSIL was observed most often in 49-year-old patients based on age alone. When the results of other studies conducted in Israel, India and Iran are examined, it was found that HSIL was observed most often at 38.6; 40.5 and 52.0 years, respectively.[10] When evaluated according to year in our study, HSIL was observed most often in 2007 (0.21%).

The smear results which contained abnormal glandular cells comprised 0.56% in our study. In our country, the incidence of AGS was determined to be 0.08% in a study with many cases.[15] The rate of glandular cell abnormalities was determined as 0.27-0.8% in other studies in the literature.[19] It was observed most often in the group over 45 years of age. In our study, it was observed most often between the ages of 46-70 and is consistent with the literature.

Smear screening is performed according to the ASCCP guidelines in our country. The national associations provide support to obstetricians about current screening strategies with regular training in this regard. Smear is not performed on patients under the age of 21 except in the presence of suspicious lesions and sexual history in our country, as in the guidelines. Our results also show that the rate of abnormal smear results was lowest in this age group. Of cervical cancer cases 0.1% are known to occur in the group under 20 years of age.[5] Although the cancer rate is low, it is stated that the rate of LSIL is 5.7% and the rate of HSIL is 0.7% in this group.[21] The rate of LSIL was 0.42% in our study. HSIL or higher grade lesion was not seen in the group consisting of a total of 241 patients. Instead of implementing a screening program in this group, it is recommended that awareness of safe sex and HPV vaccination be raised among adolescents.[5] If women over the age of sixty-five have enough negative smear results, cervical cancer screening can be stopped.[5] In this study, we evaluated groups under the age of 70 with those above the age of 70 and found that the abnormal smear results were observed most often in this group. According to the 21-45 year age group, the 46-70 year age group and the age group over 71, the rates of abnormal smear results were found to be 2.10%, 2.41% and 2.85%, respectively. The reason for continuing to perform smear tests in this age group may be explained by the lack of previous negative smear results in this group or the presence of abnormal cervical findings.

The strengths of our study are the high number of patients, the presence of sufficient knowledge due to the use of the electronic record system and exclusion of patients with malignancy from the study. Moreover, our study has several limitations. Firstly, our study was designed as a retrospective study. Secondly, the histopathologic diagnosis and follow-up of the patients with abnormal smear results were not evaluated in our study. Finally, the clinical information and HPV results of the patients could not be included. As HPV screening is performed by 1st stage health organisations (general practitioners, cancer screening centres) in Turkey, routine HPV screening is not performed at our clinic. In situations with clinical indications and cytological screening, HPV screening is performed.

In conclusion, the prevalence of cervical cytological abnormality was 2.27%. The data from our hospital over 10 years is compatible with data from various centres around the world and the country, except for the increase in the incidence of abnormal smears

in older age groups. The reduction in the incidence of cervical cancer was achieved by the dissemination of screening policies and this proves the importance of cervical protection. Further prospective studies are needed to determine the prevalence of abnormal cervical cytology results.

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