



Why are cervical smear abnormalities frequency increasing in Turkey?

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Objective: To evaluate the prevalence of abnormal cervical cytological results in Turkey. **Methods:** This retrospective case-control study was conducted in the Departments of Obstetrics and Gynecology at Sorgun State Hospital in Yozgat, Turkey between January 2015 and June 2016. Evaluation in this study was made of patients who accepted the gynecologic examination, were aged 18-75 years, were not in the menstrual period, had not had a PAP smear with in the previous year and were sexually active. The Bethesda system was used for the cervical smear sample collection, examination, and reporting. **Results:** Cervical dysplastic changes were observed in 110 cases, of which, 89 (80.90%) were diagnosed as ASCUS, 2 (1.81%) as ASC-H, 8 (7.27%) as LSIL, 2 (1.81%) as HSIL, 5 (4.54%) as AGC-NOS, 3 (2.72%) as ASCUS+AGC-NOS, and 1 (0.9%) as HSIL+AGC-NOS. The rate of abnormal Pap test result was determined as 8.02 %. **Conclusion:** The higher results could be attributed to greater sensitivity of pathologists to smear assessments or that the population could be more polygamous than expected or a combination of both.

INTRODUCTION

Cervical cancer is the second most common cancer worldwide, responsible for approximately 270,000 deaths per year, with more than 85% of these reported in under developed and developing countries in 2012.^{1,22} In 2012, an estimated 445,000 new cases were reported in less-developed regions, which constituted 84% of the new cases worldwide. Cervical cancer is the third most common gynecological cancer and the ninth most common female cancer in Turkey.^{2,23}

The Papanicolaou (Pap) smear was first described in 1943, and since the 1945 introduction of the Pap smear for cancer screening, the incidence and mortality of cervical cancer has been successfully decreased. This reduction in mortality is due to an increase in the detection of invasive cancer at early stages and the detection and treatment of pre-invasive lesions.³ However, there is a wide discrepancy between countries in the rates of screening for cervical cancer with the average screening coverage rate in high-income countries at 63% compared to 19% in low-income countries.⁴

Before 2014 in Turkey, women aged 35 – 40 years were supposed to have cervical cancer screening at least once and the Pap smear test repeated at 5-year intervals, with final screening at the age of 65 years when the last two tests are negative. The screening program was redesigned in 2014,⁵ to include a revamped local call and recall strategy and a centralized and fully automated monitoring of individual screening status, with HPV tests as the primary screening instrument, and clear national algorithms.⁶ In the last population-based cervical cytology

screening study in Turkey in 2010, Sengul D. et al. showed that the prevalence of abnormal cervical cytologies was 1.83 % in Giresun.⁷

MATERIAL-METHOD

This retrospective case-control study was conducted in the Departments of Obstetrics and Gynecology at Sorgun State Hospital in Yozgat, Turkey between January 2015 and June 2016. Informed consent was obtained from patients before the procedure. The authors declare no conflict of interest. All Pap tests were retrieved by one gynecologist and evaluated by a single pathologist. Data were collected from the medical records of participants who attended for a cervical cancer screening test or were admitted to the Obstetrics and Gynaecology Outpatient Clinic. Evaluation in this study was made of patients who accepted the gynecologic examination, were aged 18-75 years, were not in the menstrual period, had not had a PAP smear with in the previous year and were sexually active. The Bethesda system was used for the cervical smear sample collection, examination, and reporting.

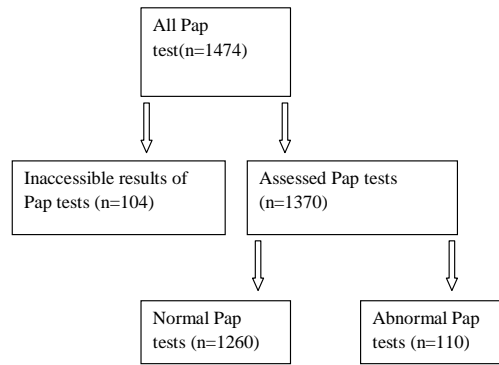
Management and analyses of the data obtained in the study were applied using SPSS software and Med Calc Statistical Software version 18.5. Differences between the study groups were determined using the χ^2 test and the Student's t test. Continuous variables were stated as mean, Standard deviation, min, max and median values, and categorical variables as number (n) and percentage (%). Chi-square analysis was used for categorical inter-variance analyses and the Fisher Freeman Halton test was used when appropriate. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

A total of 1474 Pap tests were retrieved by one gynecologist and 1370 Pap tests were evaluated by one pathologist. The remaining 104 Pap tests were evaluated in Yozgat State Hospital as the pathologist was not in Sorgun State Hospital, so the data of those tests were not included in

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The study flow chart

Table 1 Smear result- Age relationship

Smear Result (N)	Age Mean \pm Standard Deviation (Min-Max)
Normal (1260)	37.79 \pm 12.609 (18-75)
ASCUS (89)	38.86 \pm 10.68 (18-65)
LSIL(8)	36.88 \pm 11.57 (21-54)
AGC-NOS(5)	40.20 \pm 8.41 (27-48)
ASCUS + AGC-NOS(3)	49.33 \pm 5.03 (44-54)
ASC-H (2)	46.0 \pm 5.66 (42-50)
HSIL(2)	47.50 \pm 2.12 (46-49)
HSIL + AGC-NOS (1)	23 \pm 0 (23)

Table 2 Pregnancy- smear relationship

SMEAR		No pregnant N(%)	Pregnant N(%)	p
		AGC-NOS	5(0.38)	
	ASC-H	2(0.15)	0(0)	
	ASCUS	88(6.64)	1(2.33)	
	ASCUS + AGC-NOS	3(0.23)	0(0)	
	HSIL + AGC-NOS	1(0.08)	0(0)	
	HSIL	2(0.15)	0(0)	
	LSIL	8(0.6)	0(0)	
	Normal	1218(91.86)	42(97.67)	

Fisher Freman Halton Test

Table 3 Age- Pregnancy-IUD and smear relation

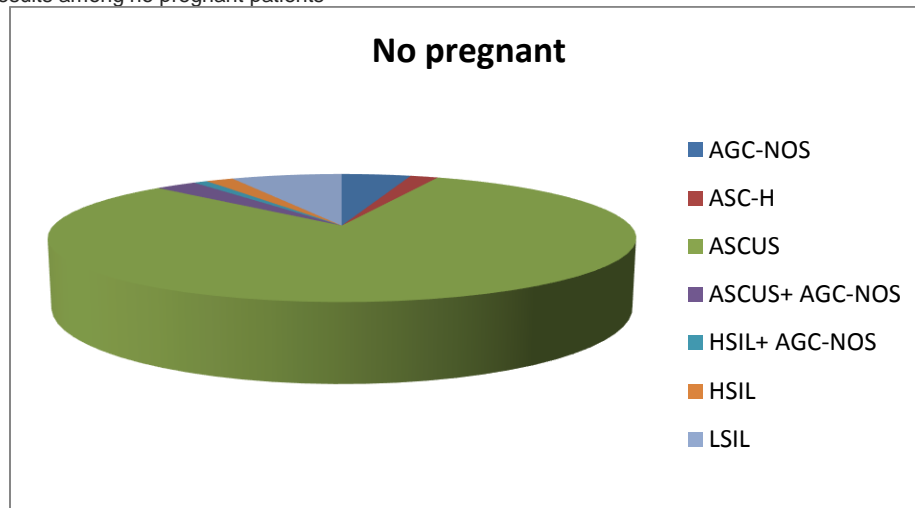
		Age \leq 30	30 -49 Age	Age \geq 50	p
		N(%)	N(%)	N(%)	
Pregnancy	No	403(30.36)	677(51.01)	247(18.61)	0.006*
	Yes	18(41.86)	25(58.14)	0(0)	
Smear	AGC-NOS	1(20)	4(80)	0(0)	0.294*
	ASC-H	0(0)	1(50)	1(50)	
	ASCUS	20(22.47)	54(60.67)	15(16.85)	
	ASCUS + AGC-NOS	0(0)	1(33.33)	2(66.67)	
	HSIL + AGNOS	1(100)	0(0)	0(0)	
	HSIL	0(0)	2(100)	0(0)	
	LSIL	2(25)	5(62.5)	1(12.5)	
	NM	397(31.50)	635(50.39)	228(18.09)	
IUD	VAR	76(31.15)	151(61.89)	17(6.97)	<0.0001**
	YOK	345(30.63)	551(48.93)	230(20.42)	

* Chi square test

** Fisher Freeman Halton test

Table 4 Pregnancy data

	N	Mean	Standard deviation	Median	Minimum	Maximum
Week of Pregnancy	43	7.78	3.43	6.71	4.00	20.71

Table 5 Abnormal smear results among no pregnant patients

the evaluation. The mean age was 37.79 ± 12.60 year (range, 18-75 years) of all the participants, 37.67 ± 12.77 years (range, 18-75 years) of those with a normal Pap test result and the ages of those with an abnormal Pap test result are shown in Table 1. Cervical dysplastic changes were observed in 110 cases, of which, 89 (80.90%) were diagnosed as atypical squamous cells of undetermined significance (ASCUS), 2 (1.81%) as high-grade lesions that cannot be excluded (ASC-H), 8 (7.27%) as low-grade squamous intraepithelial lesion (LSIL), 2 (1.81%) as high-grade squamous intraepithelial lesion (HSIL), 5 (4.54%) as atypical glandular cells-not otherwise specified (AGC-NOS), 3 (2.72%) as ASCUS+AGC-NOS, and 1 (0.9%) as HSIL+AGC-NOS (Table 2, Table 5). The rate of abnormal Pap test result was determined as 8.02 %. Most of the patients were aged between 30 and 49 years, and the abnormal cervical smear rate was also found to be higher in this age range. Of the patients in this age range, 25 were pregnant and all of these pregnant patients had normal Pap test results (Table 3). A 18-year old pregnant woman was diagnosed with ASCUS and all others had normal cytology (Table 4). There was no relationship between an intrauterine device and abnormal smear (Table 3).

DISCUSSION

The rate of invasive cervical cancer can be reduced with effective cervical cytological screening and the appropriate management of pre-invasive neoplasia as when population-based screening is available because of the long pre-invasive period.⁸

Cervical cancer is one of the most common causes of female deaths in developing countries. Therefore, early detection of this disease in the pre-cancerous stage, based on Pap smear test screening or HPV screening is of the utmost importance, especially in Muslim countries. Maleki et al. reported that cervical dysplastic changes were observed in 173 cases (4.04%), of which 81 cases (47.2%) were diagnosed as ASCUS, 40 (23%) as ASC-H, 43 (24.7%) as LSIL, 6 (3.46%) as HSIL, and 3 (1.73%) as atypical glandular cells (AGC) changes.⁹ Of studies conducted in Muslim countries, a study of 6024 Pap smear samples in

Tabriz reported the prevalence of cervical dysplasia as 1.02%.¹⁰ Another review of 13,315 Pap smear samples in Tehran, found a 1.8% incidence of neoplastic changes, of which 58.18% were ASCUS, 17.73% LSIL, 10.75% HSIL, 1.26% AGC, and 0.2% were reported as cervical carcinoma.^{11,12} In the current study, the rate of glandular lesions was seen to be higher than the findings of other studies in Muslim countries.

Another problem of cervical screening is that only 5% of women undergo a screening test in developing countries,¹³ studies carried out in Turkey have reported rates between 16.2%,¹⁴ and 51.32%.¹⁵ However, the Pap smear implementation rate in some developed countries has been reported as 93% for the USA,¹⁶ and 69 % for Spain.¹⁷ In the current study, evaluation was made of all patients who accepted the gynaecological examination in the Obstetrics and Gynaecology Outpatient Clinic, were aged 18-75 years, were not in the menstrual period, had not had a PAP smear with in the previous year and were sexually active. According to the 2016 data of the Turkish Statistical Institute (TUIK), 38,809 women lived in Sorgun, Yozgat, of whom, approximately 20,000 were 18-75 years old.¹⁸ In a period of the women resident in Sorgun were screened with Pap test and 6.84% were included in the study. However, the study population included participants from other cities such as Sarikaya, Saraykent, and Cekerek, so actual scan rate is expected to be lower than 6.84%.

In Turkey, the population-based cervical cytological screening program was started in 2008⁵ but the desired level of success was not achieved. Therefore, an HPV-based screening program was introduced, including longer screening intervals, extended referral protocols, a single national centralized diagnostics laboratory, and a sustainable agreement with the diagnostics industry. This system allowing for fully traceable, real-time monitoring of visits and specimens analysed in the centralized screening program came into force in 2014.⁶ This study was conducted after the end of the cervical cytological screening program because there were no HPV tests in our hospital, only in family health centers. Therefore, population-based cervical cytology screening was continued in our department.

A study in Romania showed that among the satisfactory smears, 0.07% were classified as invasive squamous carcinoma and 0.04% as invasive adenocarcinoma.¹⁹ In Turkey, 0.08% of smears have been reported as invasive squamous carcinoma and 0.02% as invasive adenocarcinoma.⁵ In Croatia and Italy, respectively, 0.4% and 0.01% of smears have been determined as squamous carcinoma.^{20,21} In 2014, Sengul D et al. studied 32578 Pap test results and reported that overall, prevalence of cytological abnormality was 1.83% (n=598), with ASCUS in 1.18% (n=386), LSIL in 0.39% (n=127), HSIL in 0.16% (n=53), AGC in 0.07% (n=23), squamous cell carcinoma in 0.02% (n=7), and adenocarcinoma in 0.006% (n=2).⁷ There were no results of cancers in the current study among Pap test results.

CONCLUSION

The results of this study showed that the rate of abnormal cervical smears was higher in Sorgun than previous study findings reported in Turkey. This raises the question of the reason for this situation. It could be attributed to greater sensitivity of pathologists to smear assessments or that the population could be more polygamous than expected or a combination of both. The study's limitations are both one pathologist evaluated the Pap tests and there was no data of HPV status and cervical biopsy results.

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Authors Contributions

Cihan Comba - contributed to the whole article.
Omer Demir - prepared manuscript.

Conflict of interest

All of author declare that we have no conflict of interest in connection with this paper.

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